



2 100 101 102 103 104 105 106 107 108 109 100 101 102 103 104 105

FIG. 1A

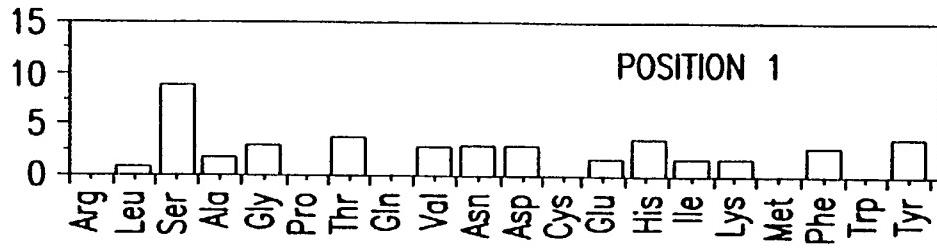


FIG. 1B

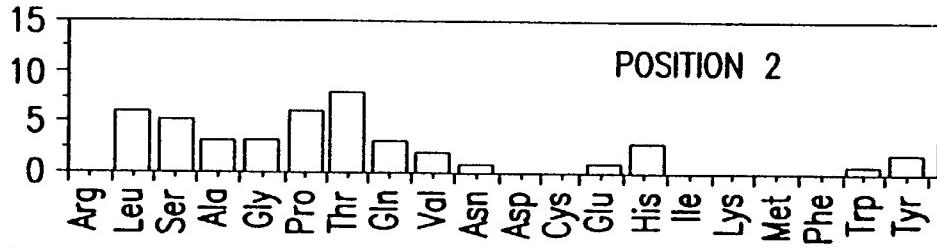


FIG. 1C

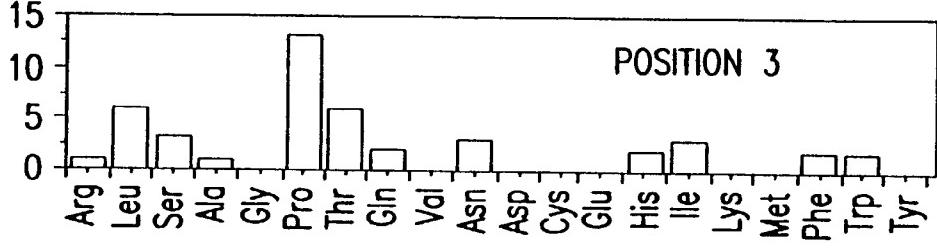


FIG. 1D

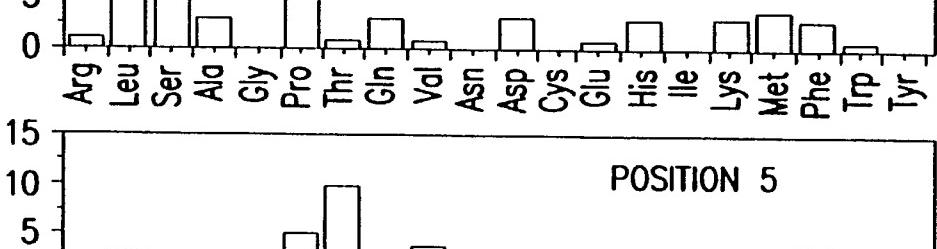


FIG. 1E

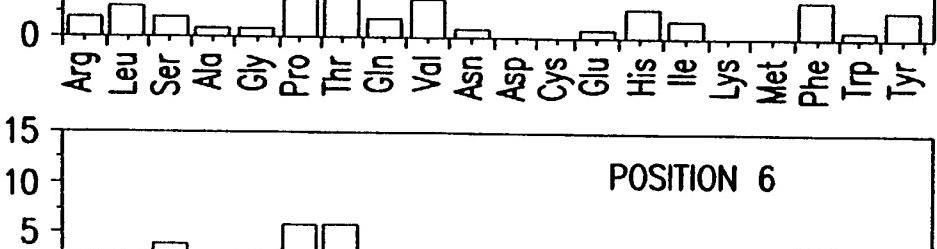


FIG. 1F

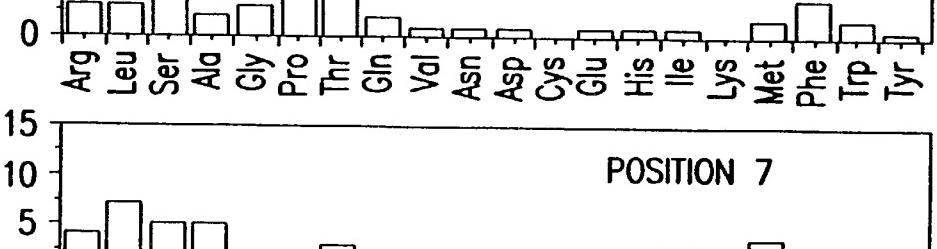
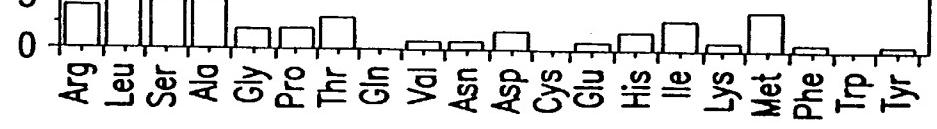


FIG. 1G





2 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0

His Thr Thr Val Tyr Gly Ala Gly
CAT ACG ACT GTT TAT GGG GCT GGT

Thr Glu Thr Pro Tyr Pro Thr Gly
ACT GAG ACG CCT TAT CCT ACT GGT

Leu Thr Thr Pro Phe Ser Ser Gly
CTT ACT ACT CCG TTT TCG TCG GGT

Gly Val Pro Leu Thr Met Asp Gly
GGT GTG CCT CTT ACG ATG GAT GGT

Lys Leu Pro Thr Val Leu Arg Gly
AAG CTT CCG ACT GTT CTG CGG GGT

Cys Arg Phe His Gly Asn Arg Gly
TGT CGC TTT CAT GGG AAT CGT GGT

Tyr Thr Arg Asp Phe Glu Ala Gly
TAT ACT CGG GAT TTT GAG GCT GGT

Ser Ser Ala Ala Gly Pro Arg Gly
TCG TCG GCG GCT GGT CCG CGG GGT

Ser Leu Ile Gln Tyr Ser Arg Gly
TCT CTG ATT CAG TAT TCG AGG GGT

Asp Ala Leu Met Trp Pro UKN Gly
GAT GCT CTT ATG TGG CCT NTG GGT

Ser Ser UKN Ser Leu Tyr Ile Gly
TCG TCT CNT TCG TTG TAT ATT GGT

Phe Asn Thr Ser Thr Arg Thr Gly
TTT AAT ACT TCG ACG CGT ACG GGT

Thr Val Gln His Val Ala Phe Gly
ACT GTG CAG CAT GTT GCT TTT GGT

Asp Tyr Ser Phe Pro Pro Leu Gly
GAT TAT TCT TTT CCG CCT CTT GGT

Val Gly Ser Met Glu Ser Leu Gly
GTG GGG TCT ATG GAG TCG TTG GGT

Phe UKN Pro Met Ile UKN Ser Gly
TTT CAN CCG ATG ATT NGN TCG GGT

Ala Pro Pro Arg Val Thr Met Gly
GCG CCT CCG CGG GTT ACT ATG GGT

FIG.1H



J 10 0 3 5 2 3 7 3 3 3 3 0 2 3 3 0 2 3

Ile Ala Thr Lys Thr Pro Lys Gly
ATT GCT ACG AAG ACG CCT AAG GGT

Lys Pro Pro Leu Phe Gln Ile Gly
AAG CCT CCG TTG TTT CAG ATT GGT

Tyr His Thr Ala His Asn Met Gly
TAT CAT ACT GCT CAT AAT ATG GGT

Ser Tyr Ile Gln Ala Thr His Gly
TCT TAT ATT CAG GCT ACG CAT GGT

Ser Ser Phe Ala Thr Phe Leu Gly
TCG TCT TTT GCT ACT TTT CTT GGT

Thr Thr Pro Pro Asn Phe Ala Gly
ACG ACT CCG CCG AAT TTT GCG GGT

Ile Ser Leu Asp Pro Arg Met Gly
ATT TCT CTT GAT CCG CGT ATG GGT

Ser Leu Pro Leu Phe Gly Ala Gly
TCG CTG CCG CTG TTT GGT GCG GGT

Asn Leu Leu Lys Thr Thr Leu Gly
AAT CTT CTT AAG ACT ACG CTT GGT

Asp Gln Asn Leu Pro Arg Arg Gly
GAT CAG AAT CTG CCG CGG CGG GGT

Ser His Phe Glu Gln Leu Leu Gly
AGT CAT TTT GAG CAG CTG CTT GGT

Thr Pro Gln Leu His His Gly Gly
ACG CCG CAG CTT CAT CAT GGT GGT

Ala Pro Leu Asp Arg Ile Thr Gly
GCG CCT CTG GAT AGG ATT ACG GGT

Phe Ala Pro Leu Ile Ala His Gly
TTT GCG CCT CTT ATT GCG CAT GGT

Ser Trp Ile TER Thr Phe Met Gly
TCG TGG ATT TAG ACG TTT ATG GGT

Asn Thr Trp Pro His Met Tyr Gly
AAT ACT TGG CCT CAT ATG TAT GGT

Glu Pro Leu Pro Thr Thr Leu Gly
GAG CCT CTT CCG ACT ACG TTG GGT

His Gly Pro His Leu Phe Asn Gly
CAT GGG CCT CAT CTG TTT AAT GGT

FIG.11



JL CO CO S C2 E3 P7 E3 .. JL CO E3 E3 C4 E3

Tyr Leu Asn Ser Thr Leu Ala Gly
TAT CTG AAT TCT ACG CTT GCT GGT

His Leu His Ser Pro Ser Gly Gly
CAT CTT CAT AGT CCG TCG GGG GGT

FIG.1J



FIG.2A

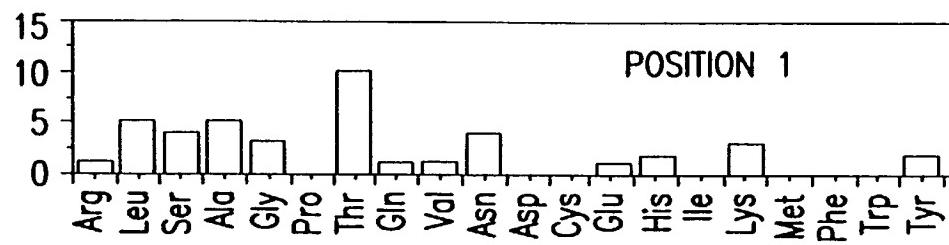


FIG.2B

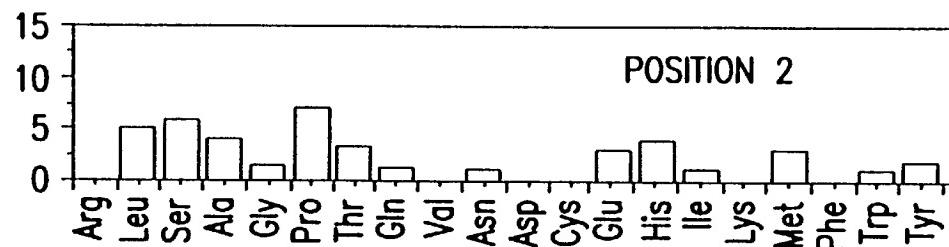


FIG.2C

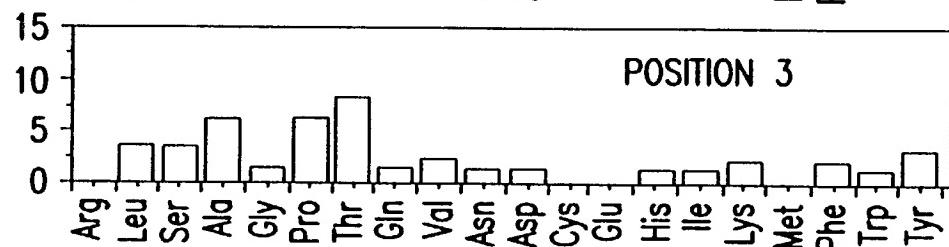


FIG.2D

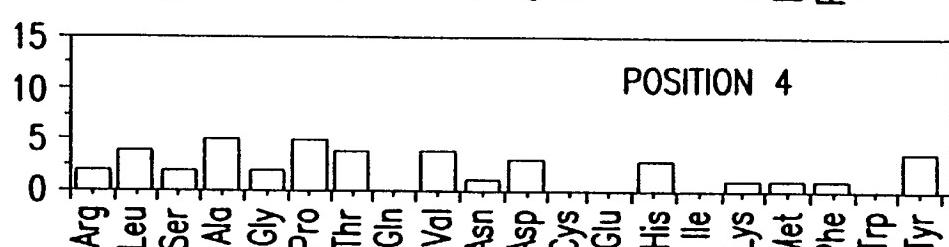


FIG.2E

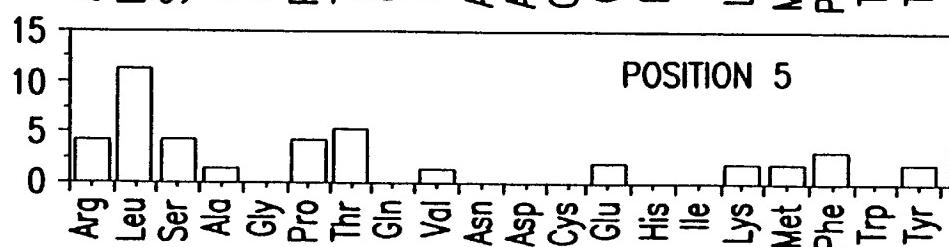


FIG.2F

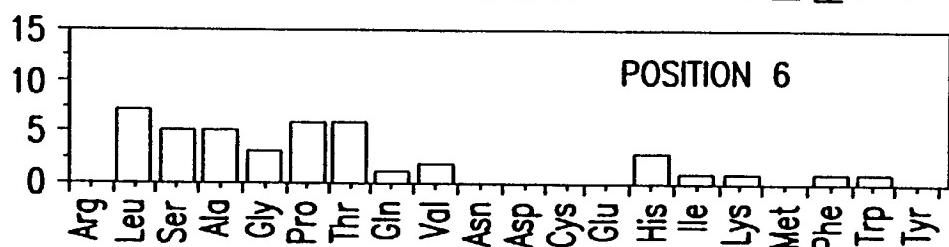
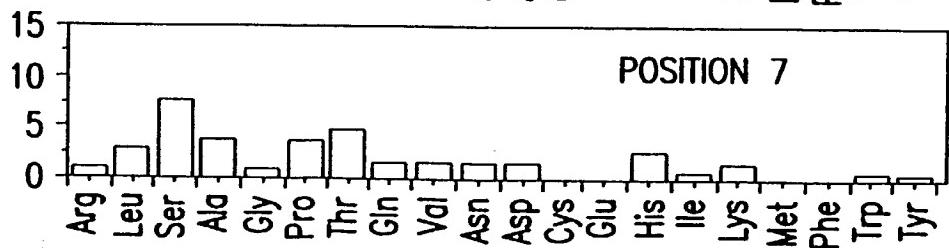


FIG.2G





Thr Leu Pro His Arg Leu Asn Gly
 ACT CTG CCT CAT CGT CTG AAT GGT

 Ser Ser Pro Arg Glu Val His Gly
 TCG AGT CCG AGG GAG GTT CAT GGT

 Asn Gln Val Asp Thr Ala Arg Gly
 AAT CAG GTT GAT ACG GCT CGG GGT

 Tyr Pro Thr Pro Leu Leu Thr Gly
 TAT CCT ACG CCG CTG CTG ACT GGT

 His Pro Ala Ala Phe Pro Trp Gly
 CAT CCT GCT GCT TTT CCT TGG GGT

 Leu Ieu Pro His Ser Ser Ala Gly
 CTT CTT CCG CAT TCT AGT GCT GGT

 Leu Glu Thr Tyr Thr Ala Ser Gly
 CTT GAG ACT TAT ACG GCT TCT GGT

 Lys Tyr Val Pro Leu Pro Pro Gly
 AAG TAT GTG CCT CTG CCG CCG GGT

 Ala Pro Leu Ala Leu His Ala Gly
 GCG CCG TTG GCT CTG CAT GCG GGT

 Tyr Glu Ser Leu Leu Thr Lys Gly
 TAT GAG TCG CTG CTG ACT AAG GGT

 Ser His Ala Ala Ser Gly Thr Gly
 TCT CAT GCG GCT TCT GGT ACT GGT

 Gly Leu Ala Thr Val Lys Ser Gly
 GGT TTG GCG ACT GTT AAG TCT GGT

 Gly Ala Thr Ser Phe Gly Leu Gly
 GGT GCT ACG TCT TTT GGG CTT GGT

 Lys Pro Pro Gly Pro Val Ser Gly
 AAG CCG CCT GGG CCG GTG TCG GGT

 Thr Leu Tyr Val Ser Gly Asn Gly
 ACT CTT TAT GTT TCT GGG AAT GGT

 His Ala Pro Phe Lys Ser Gln Gly
 CAT GCT CCG TTT AAG TCT CAG GGT

 Val Ala Phe Thr Arg Leu Pro Gly
 GTG GCG TTT ACG CGG CTT CCG GGT



Leu Pro Thr Arg Thr Pro Ala Gly
CTG CCG ACT CGT ACG CCG GCT GGT

Ala Ser Phe Asp Leu Leu Ile Gly
GCG AGT TTT GAT CTT TTG ATT GGT

Arg Met Asn Thr Glu Pro Pro Gly
CGG ATG AAT ACT GAG CCT CCG GGT

Lys Met Thr pro Leu Thr Thr Gly
AAG ATG ACT CCT CTG ACG ACT GGT

Ala Asn Ala Thr Pro Leu Leu Gly
GCG AAT GCG ACG CCT CTG CTG GGT

Thr Ile Trp Pro Pro Pro Val Gly
ACT ATT TGG CCT CCG CCT GTT GGT

Gln Thr Lys Val Met Thr Thr Gly
CAG ACT AAG GTG ATG ACG ACG GGT

Asn His Ala Val Phe Ala Ser Gly
AAT CAT GCT GTT TTT GCT AGT GGT

Leu His Ala Ala UKN Thr Ser Gly
CTG CAT GCG GCT ANT ACG TCG GGT

Thr Trp Gln Pro Tyr Phe His Gly
ACG TGG CAG CCG TAT TTT CAT GGT

Ala Pro Leu Ala Leu His Ala Gly
GCG CCG TTG GCT CTG CAT GCG GGT

Thr Ala His Asp Leu Thr Val Gly
ACG GCG CAT GAT CTG ACT GTT GGT

Asn Met Thr Asn Met Leu Thr Gly
AAT ATG ACT AAT ATG CTT ACT GGT

Gly Ser Gly Leu Ser Gln Asp Gly
GGT TCT GGG CTG TCT CAG GAT GGT

Thr Pro Ile Lys Thr Ile Tyr Gly
ACG CCG ATT AAG ACG ATT TAT GGT

Ser His Leu Tyr Arg Ser Ser Gly
TCG CAT CTG TAT CGT TCT AGT GGT

FIG.21

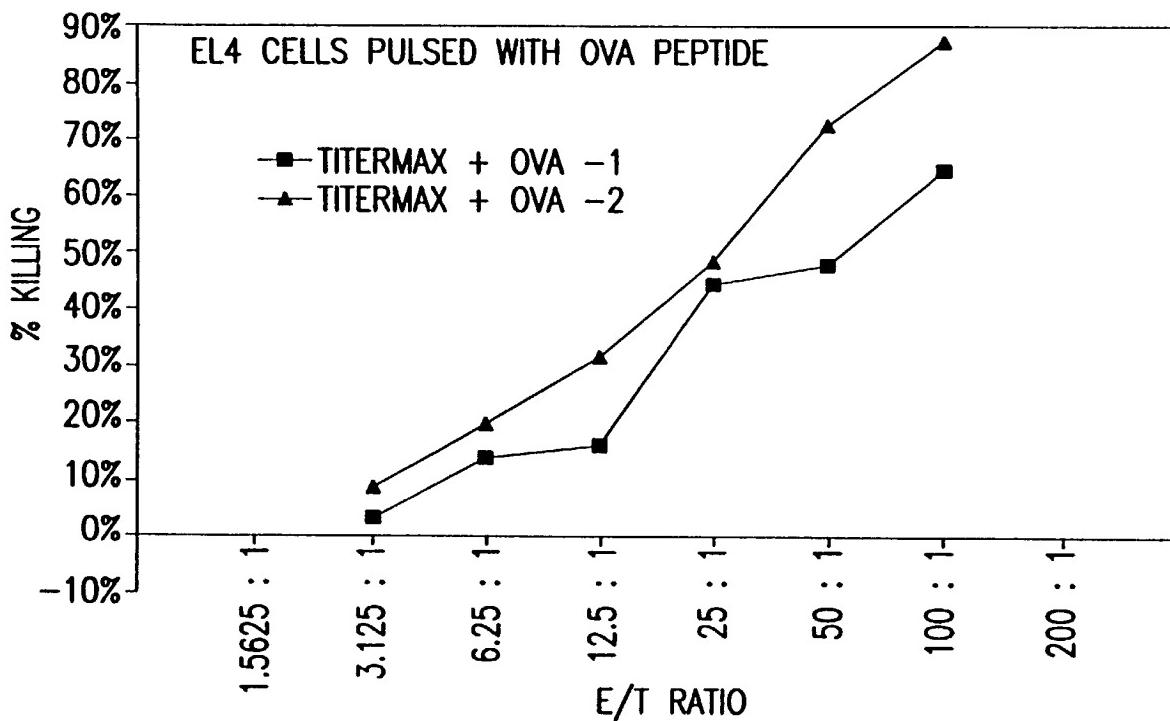


FIG. 3A

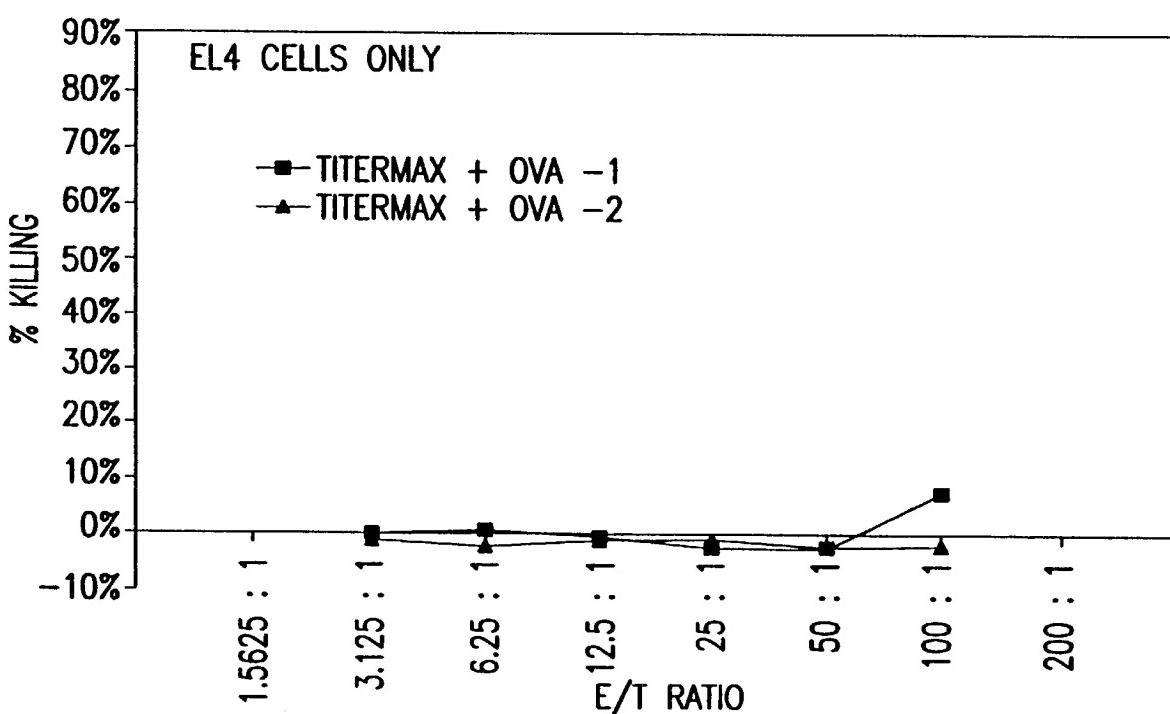


FIG. 3B



J. CLINTON E. S. T. E. S. M. J. C. D. E. S. C. P. E. S.

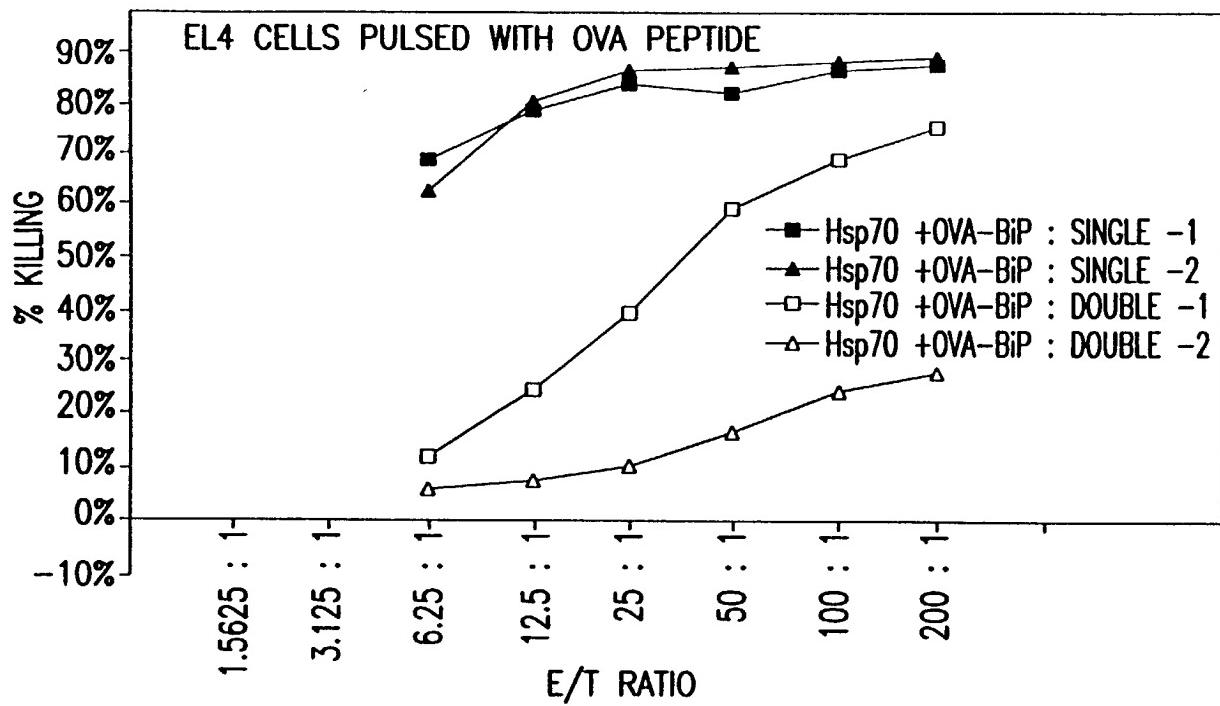


FIG.4A

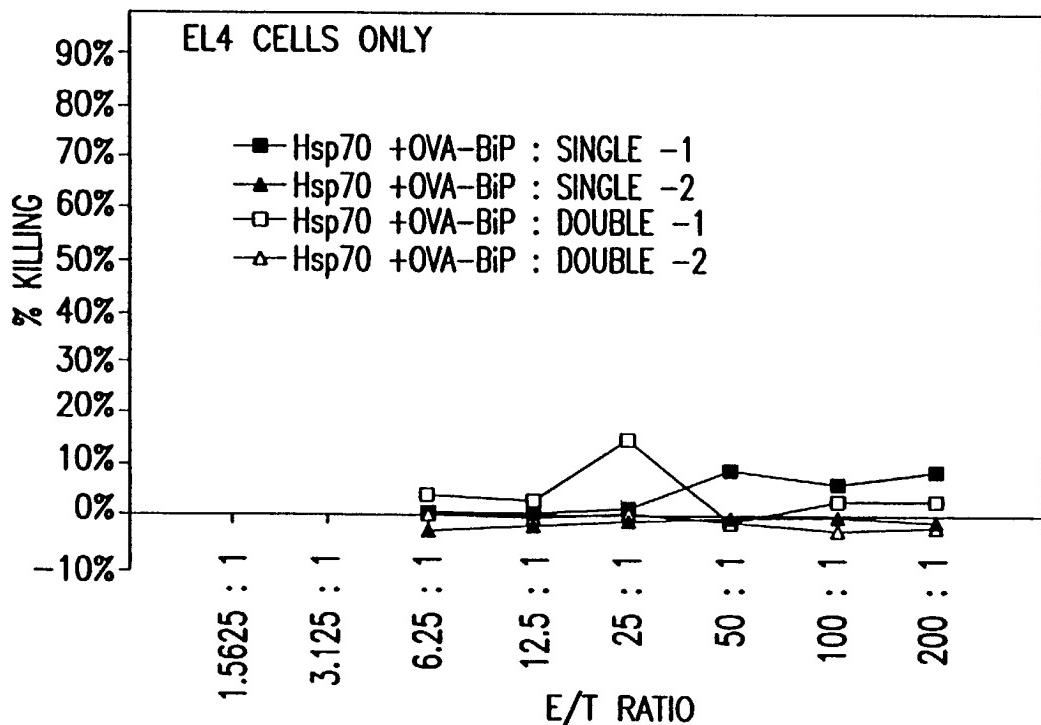


FIG.4B



1.5625 3.125 6.25 12.5 25 50 100 200 : 1

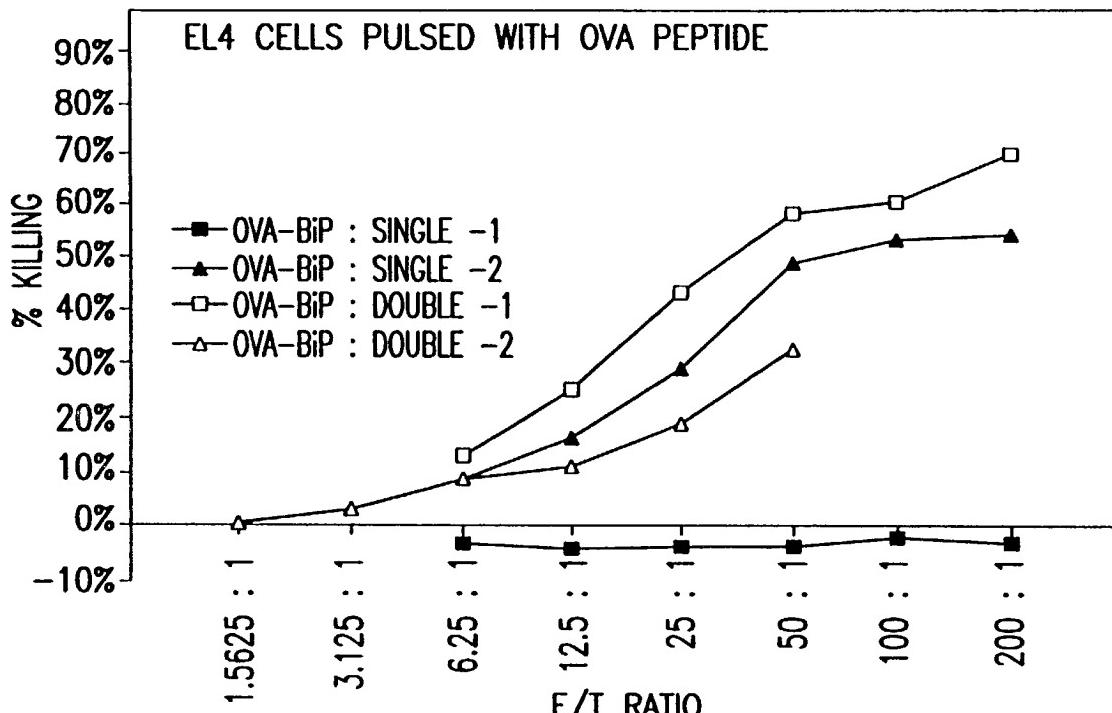


FIG.5A

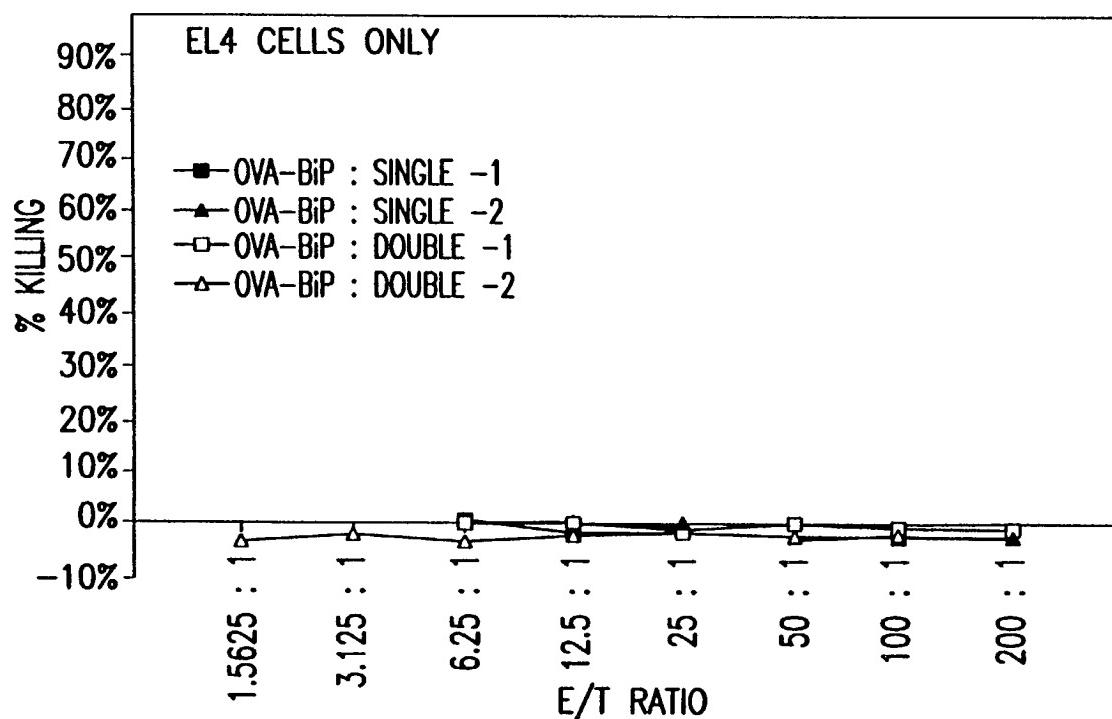
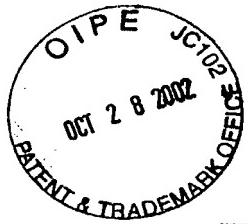


FIG.5B



JL 101 02 55 22 13 77 133 = JL 03 23 02 23

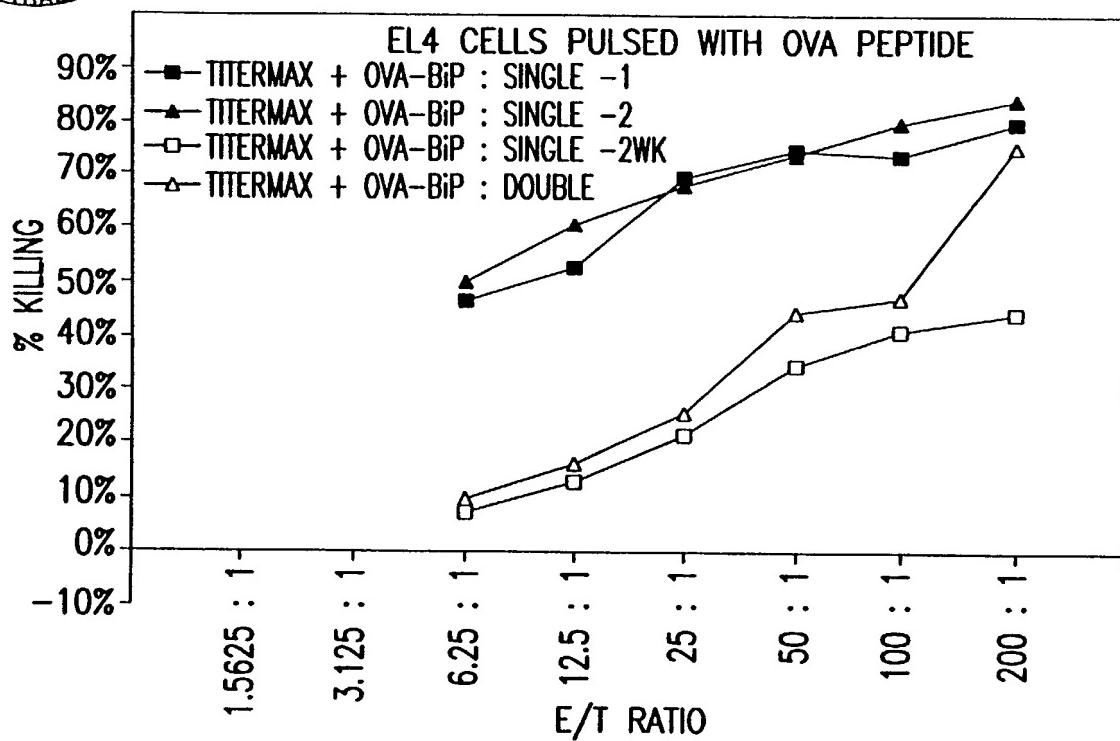


FIG.6A

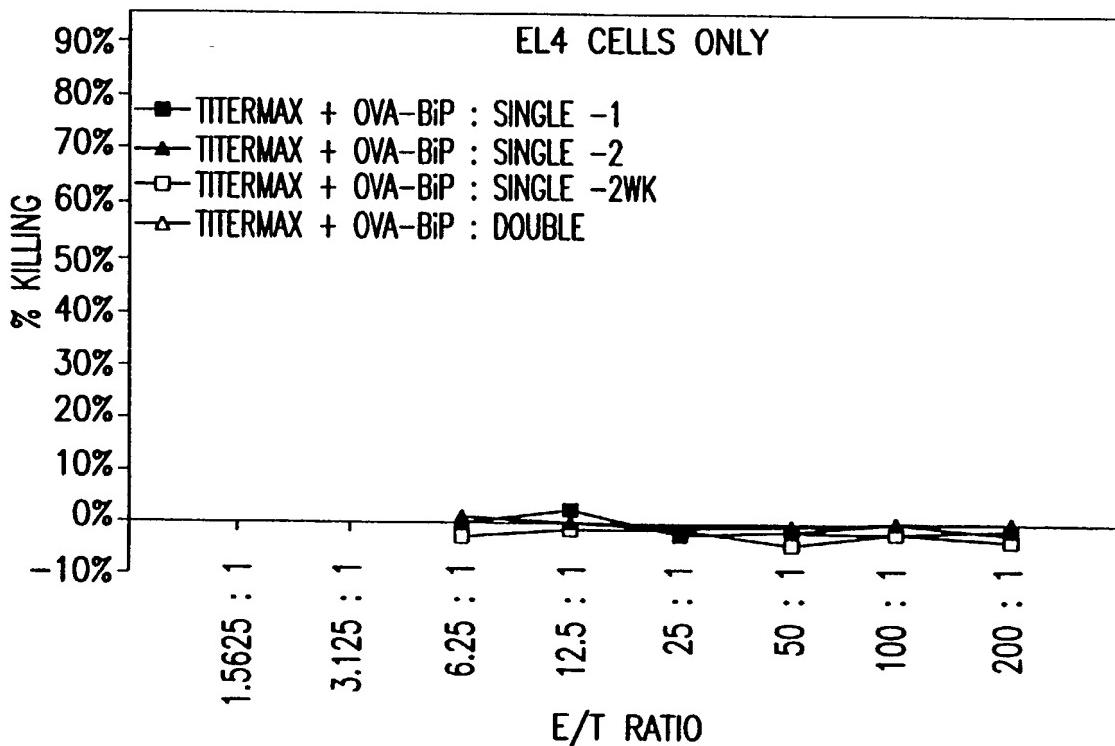


FIG.6B



3,610,023 2,237,432 3,612,330 3,612,

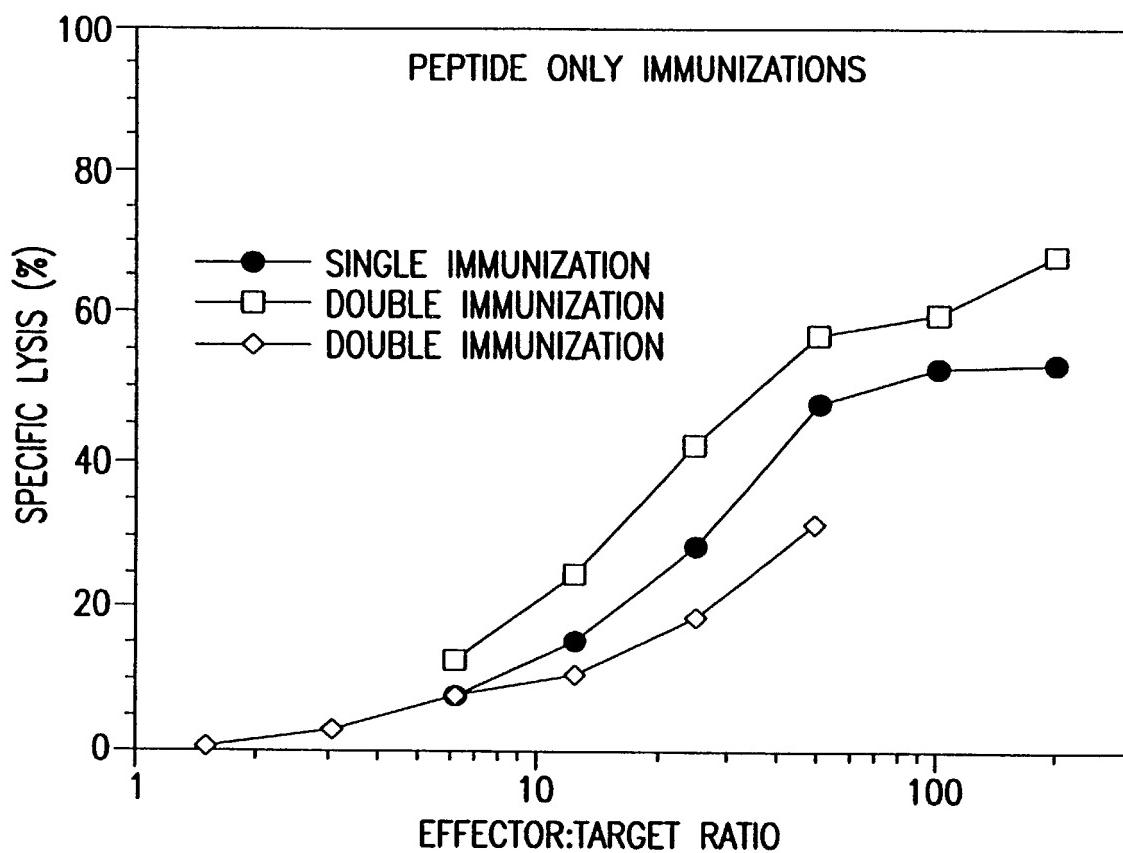


FIG.7

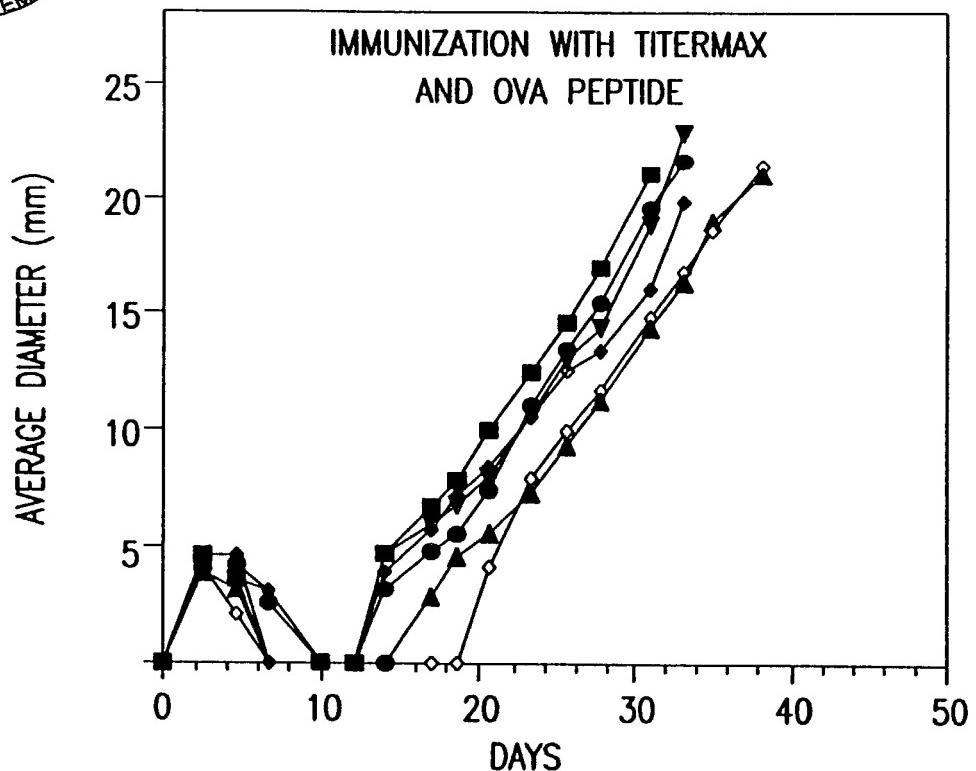


FIG.8A

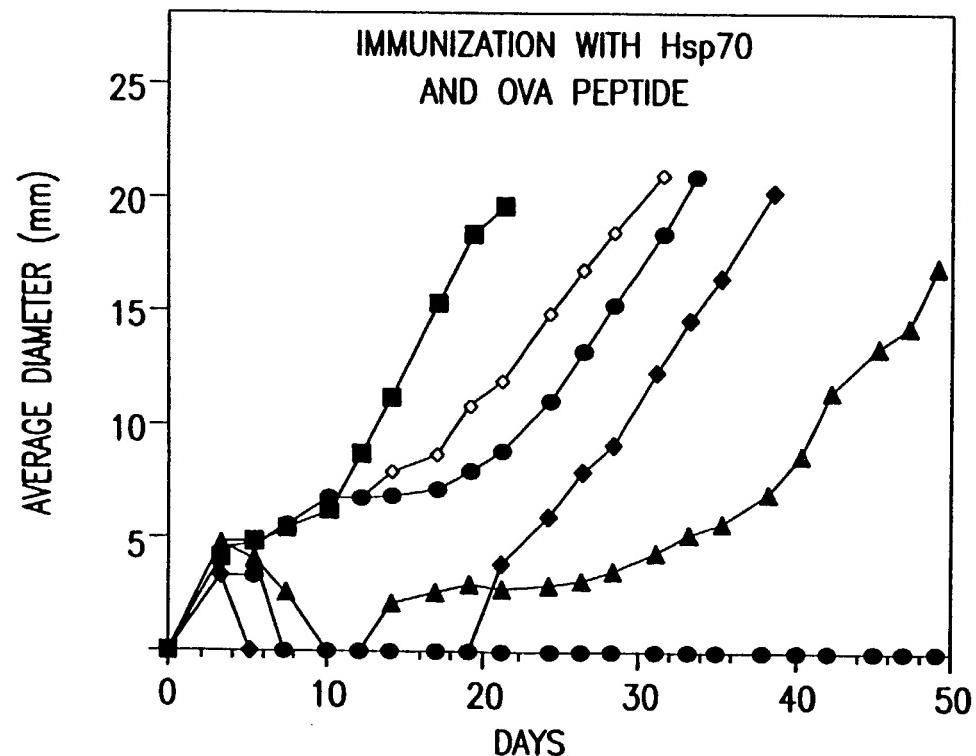


FIG.8B

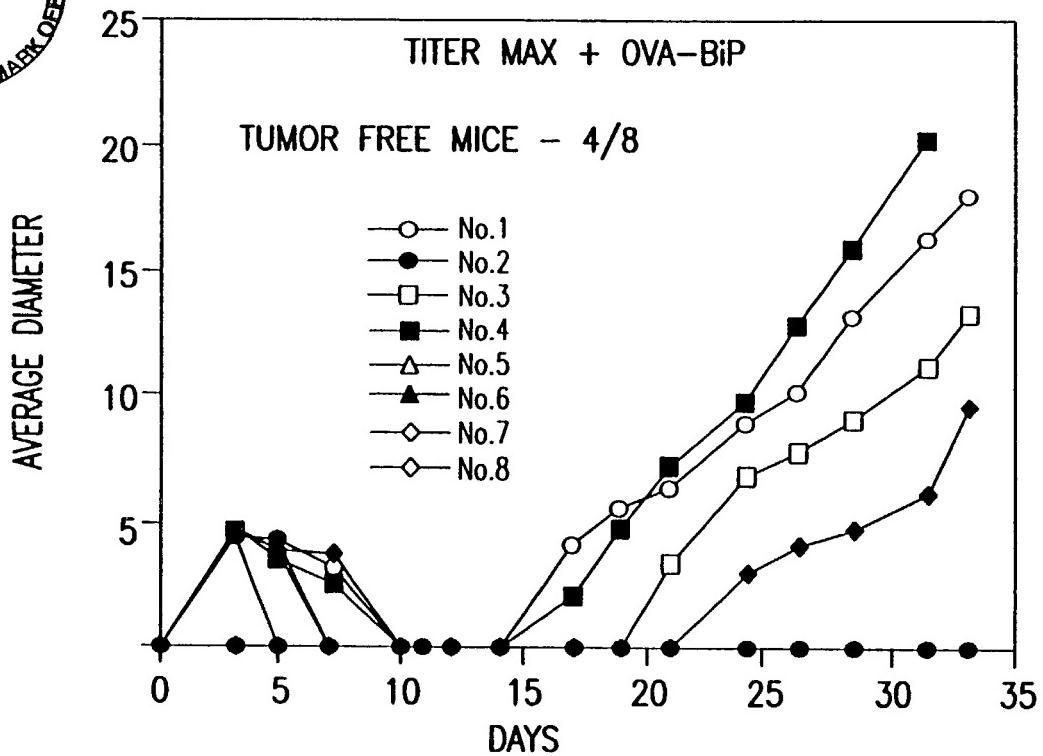


FIG.8C

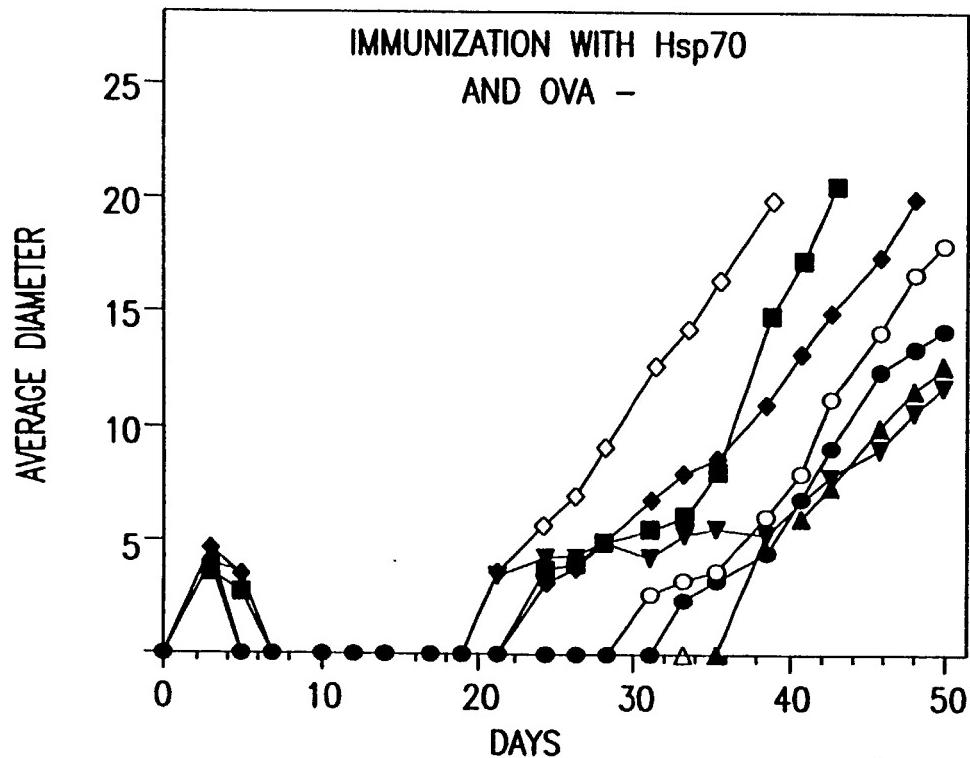


FIG.8D

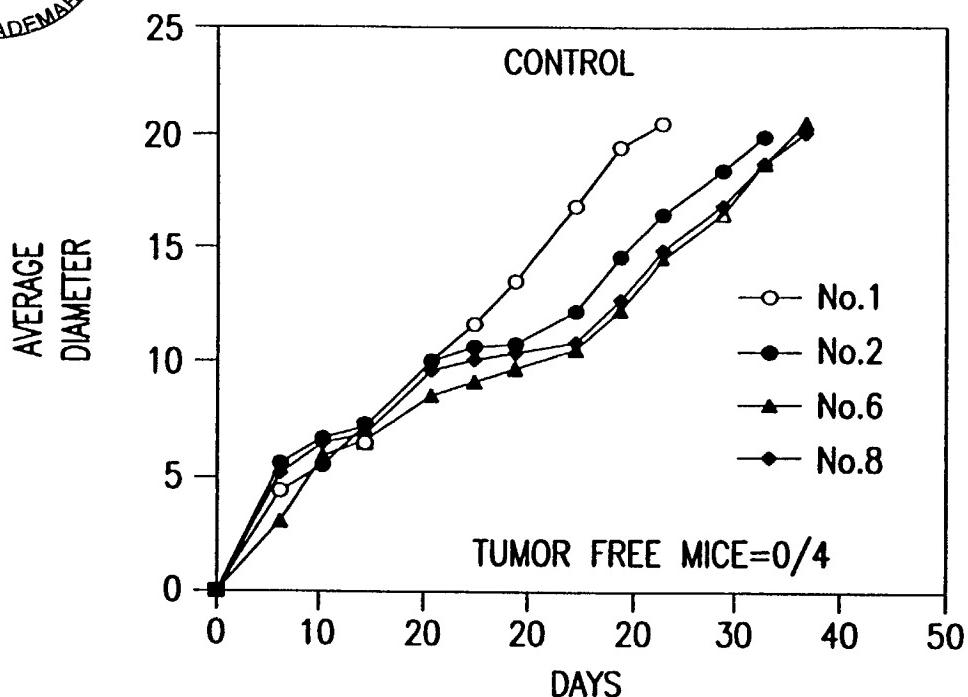


FIG.8E

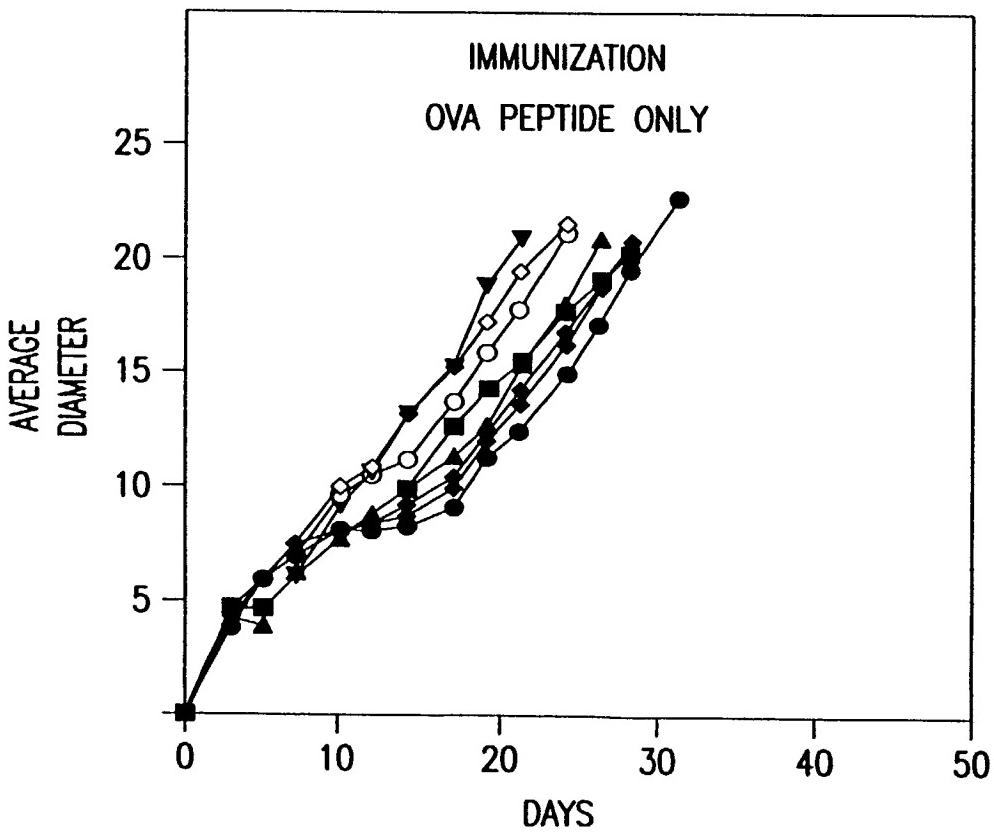


FIG.8F



31 30 01 5 22 23 27 28 .. 31 02 23 40 22

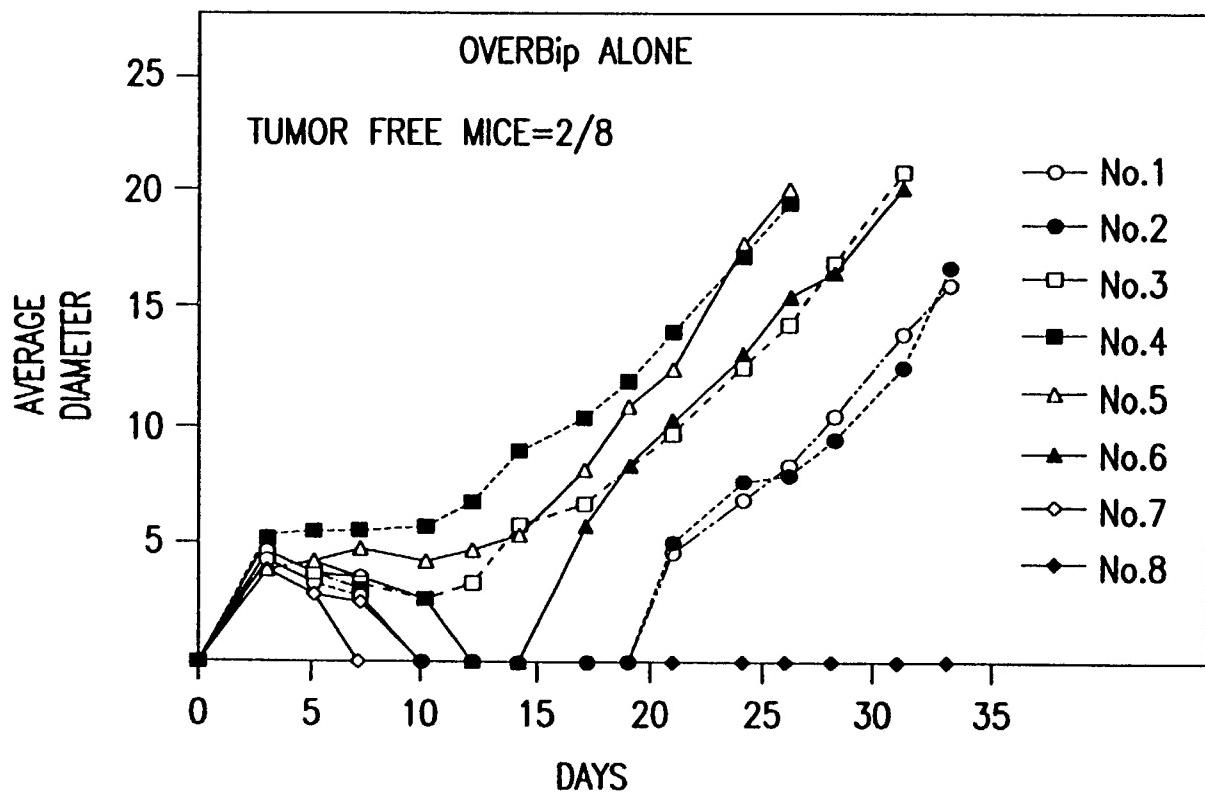


FIG.8G



1 1

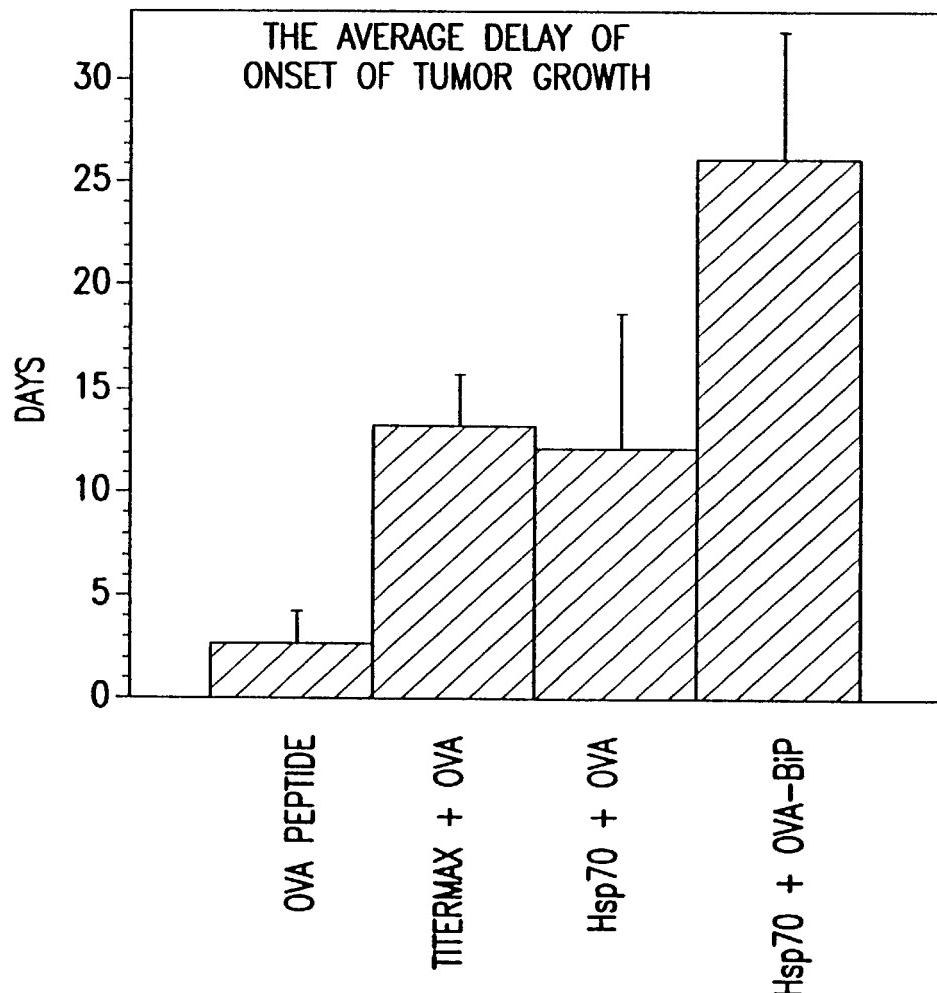


FIG.8H



J. L. O. C. E. P. E. S. P. T. E. S. A. J. C. E. P. E. S. C. E. S.

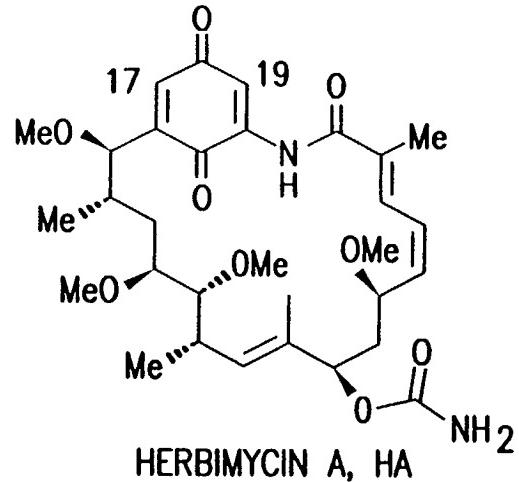
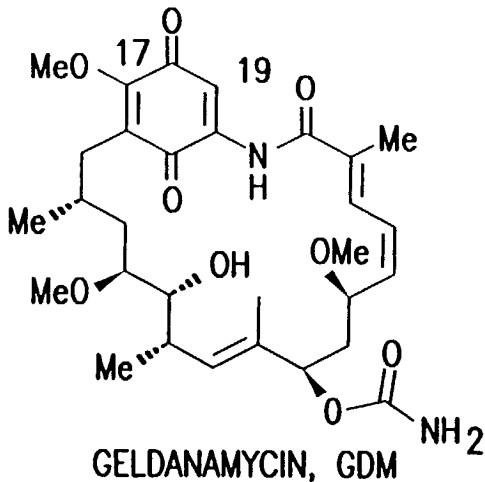


FIG.9A

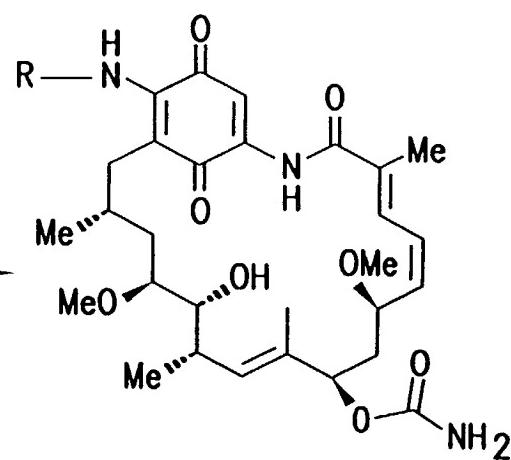
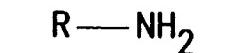
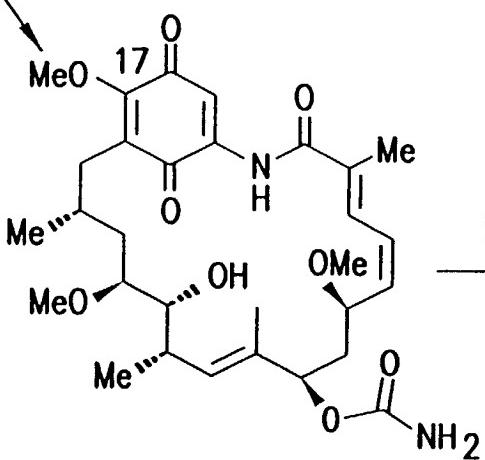
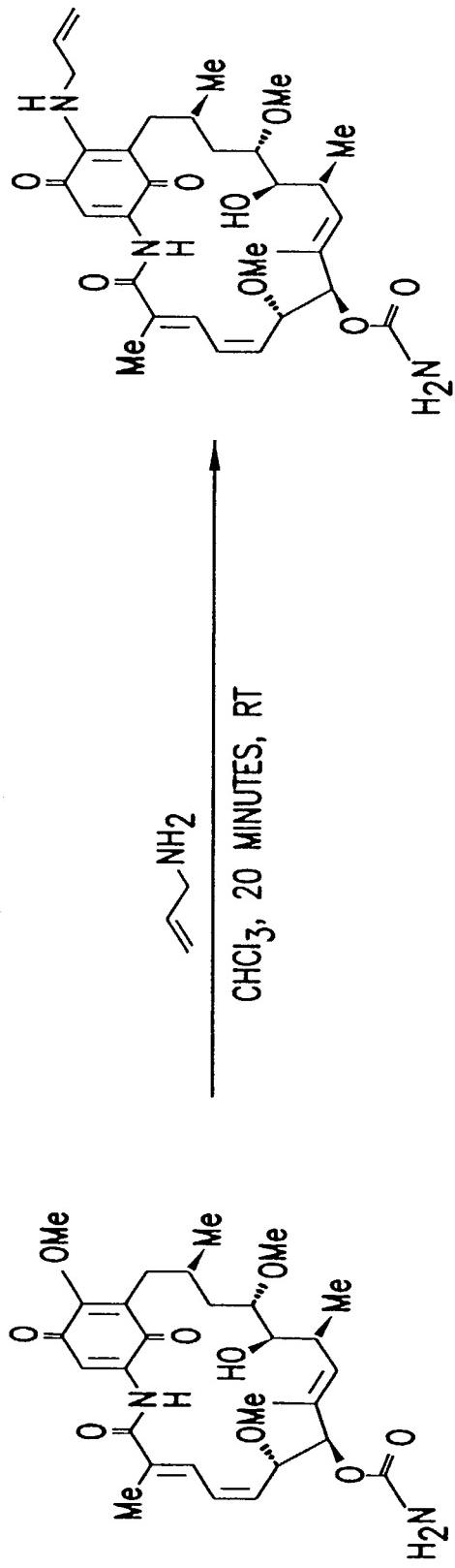
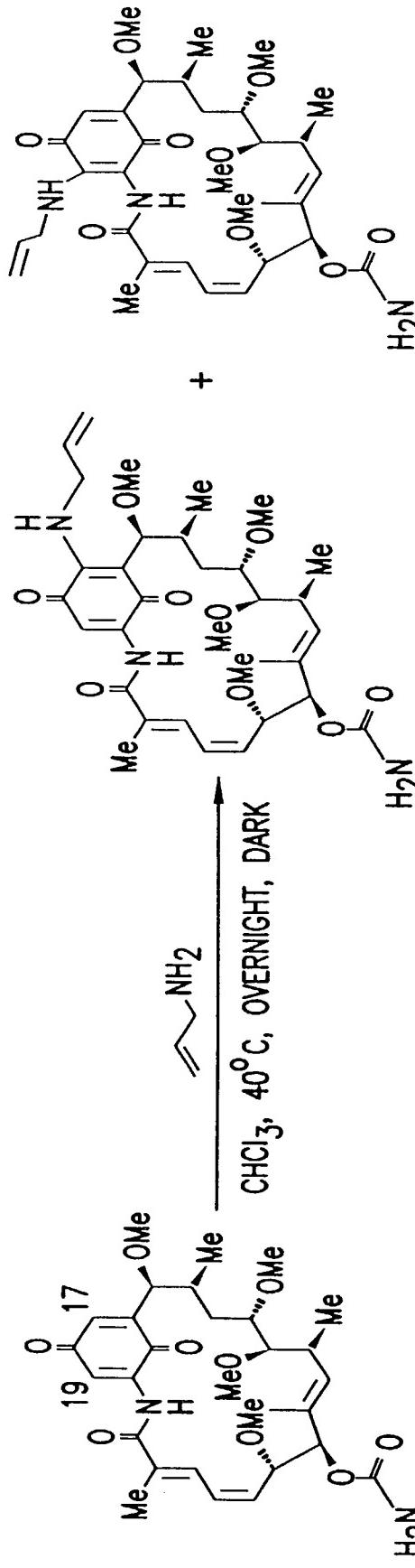


FIG.9B



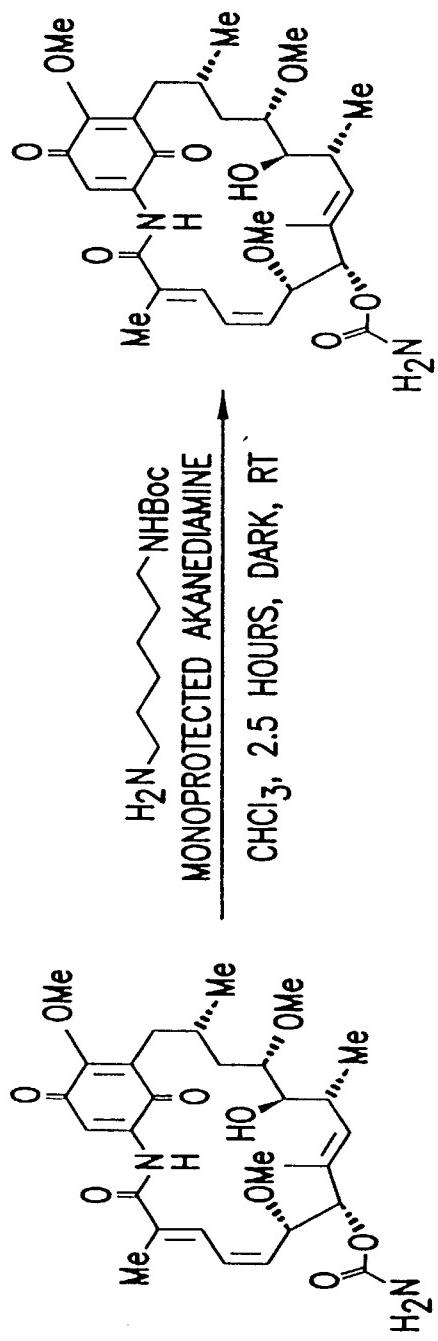
17-ALLYLAMINO-17-DEMETHOXY GDM



19-ALLYLAMINO HA
30% YIELD

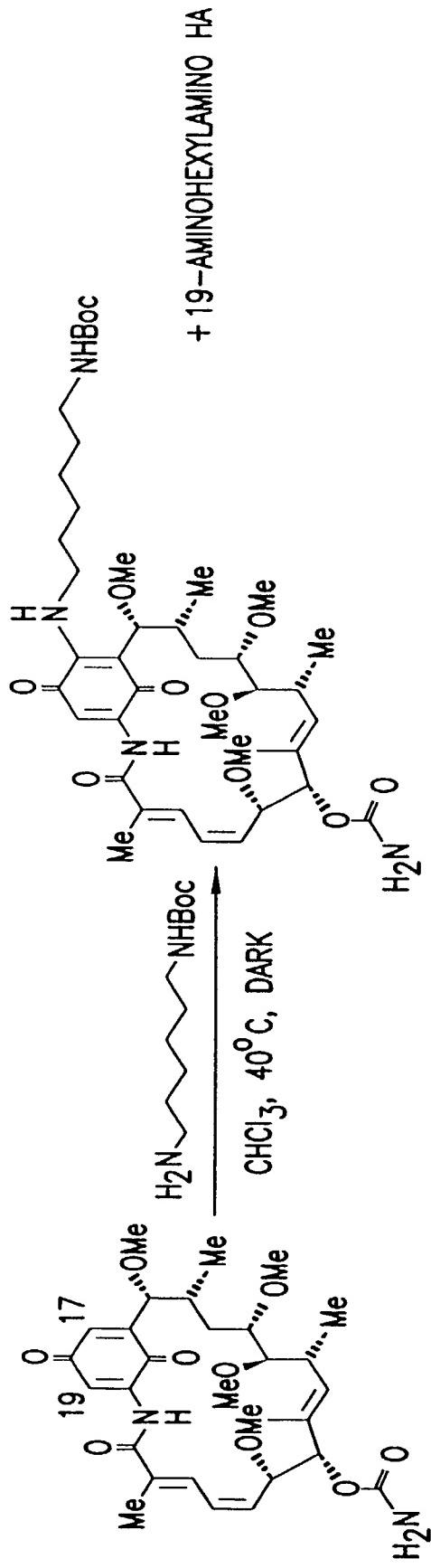
FIG. 9C

HERBIMYCIN A, HA



GELDANAMYCIN, GDM

AMINOTETHERED GDM



HERBINYCIN A, HA

17-AMINOHEXYLAMINO HA

FIG. 9D



VARIABLE SPACER, TETHER

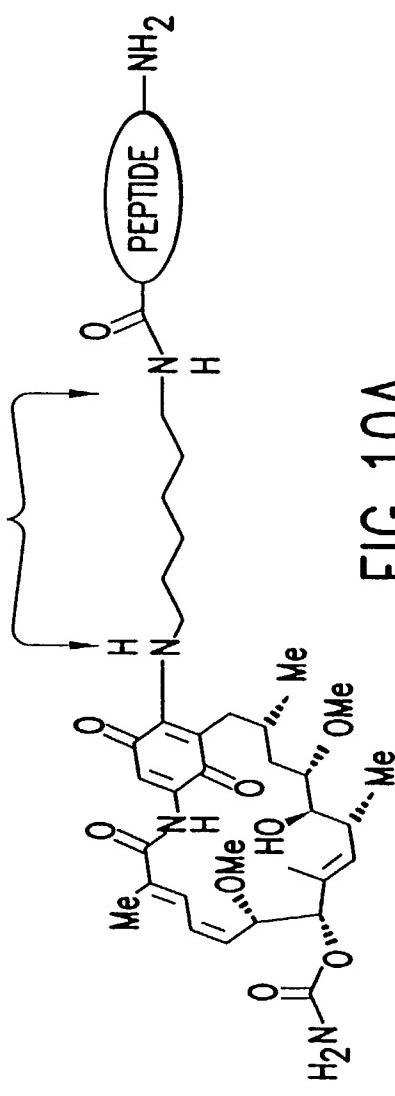


FIG. 10A

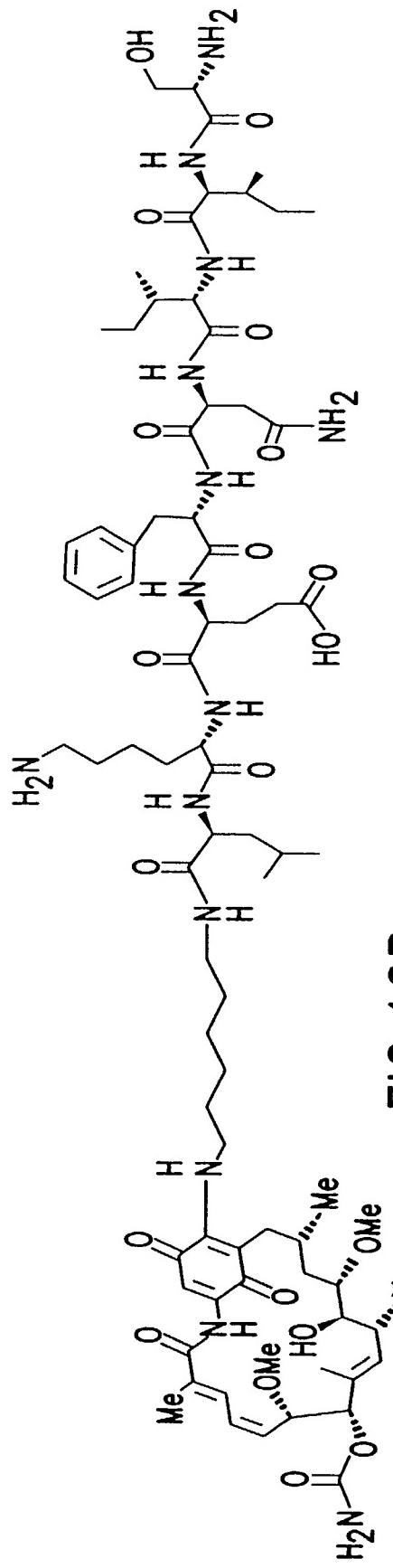
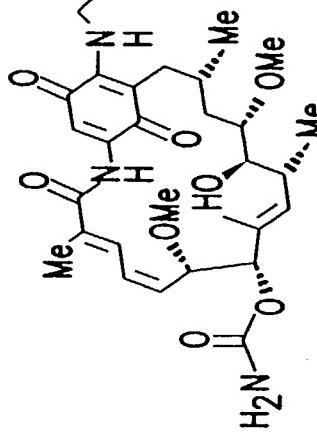
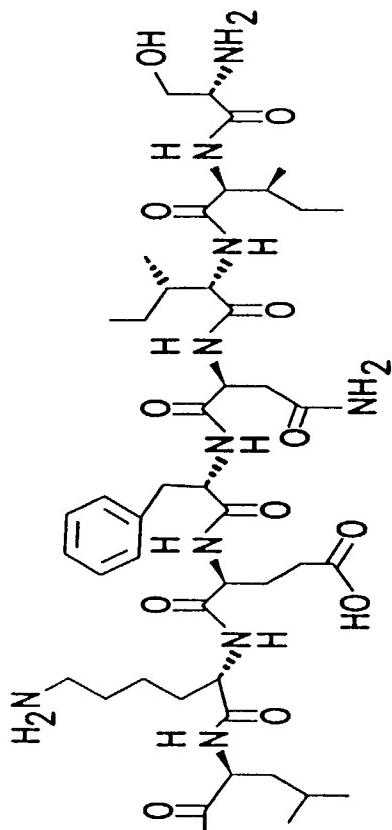
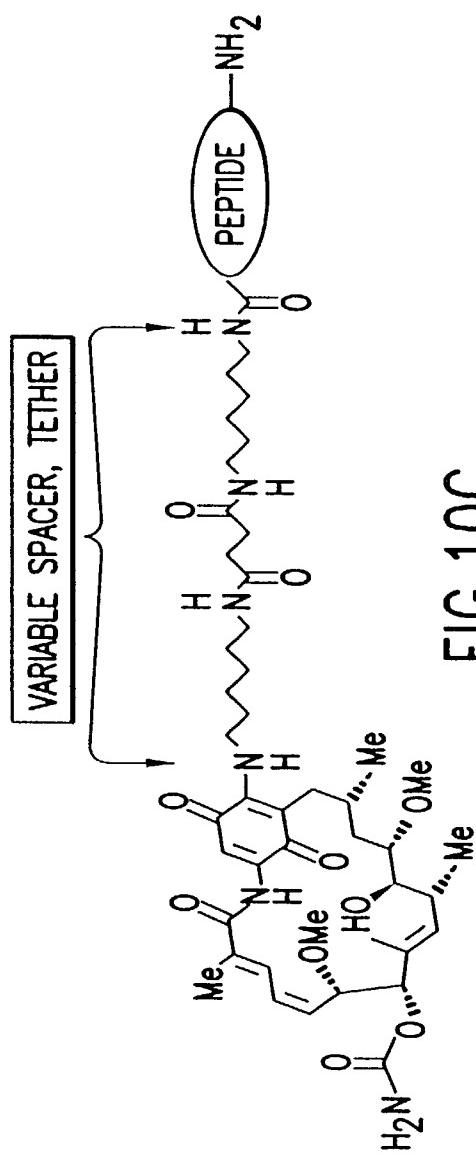


FIG. 10B





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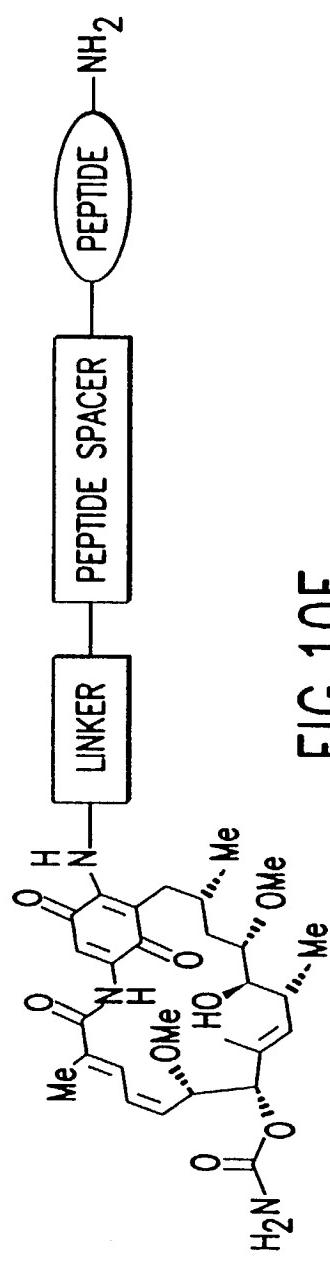


FIG. 10E

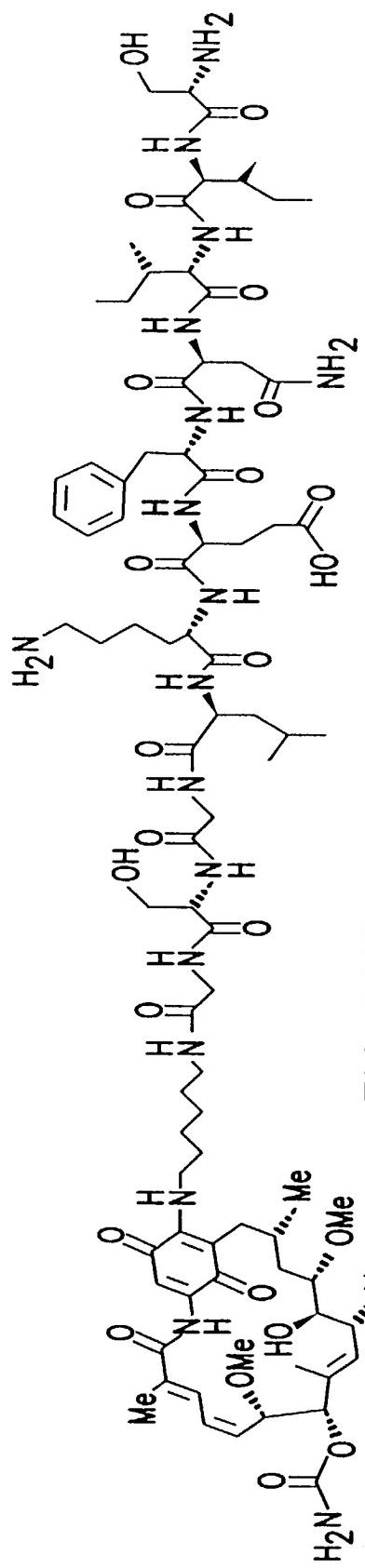


FIG. 10F



10 C 5 E 2 E 3 7 E 3 11 C 2 E 3 4 E 2

VARIABLE SPACER, TETHER

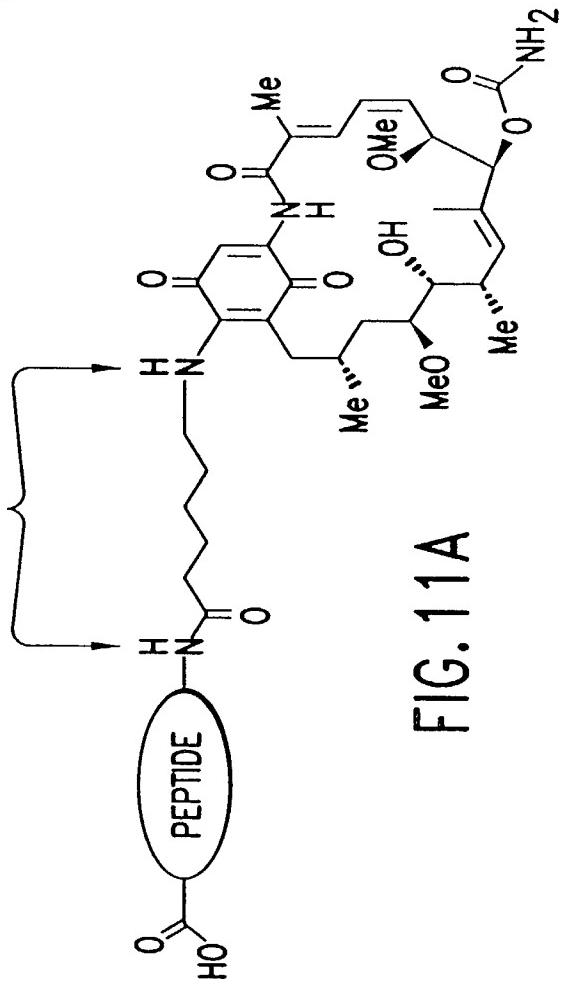


FIG. 11A

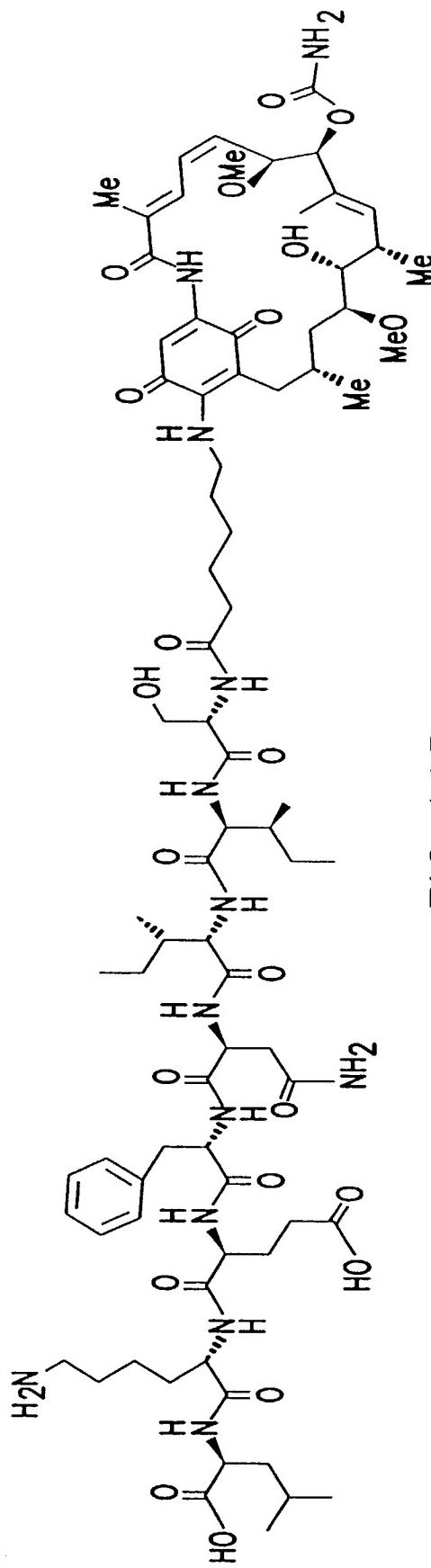


FIG. 11B

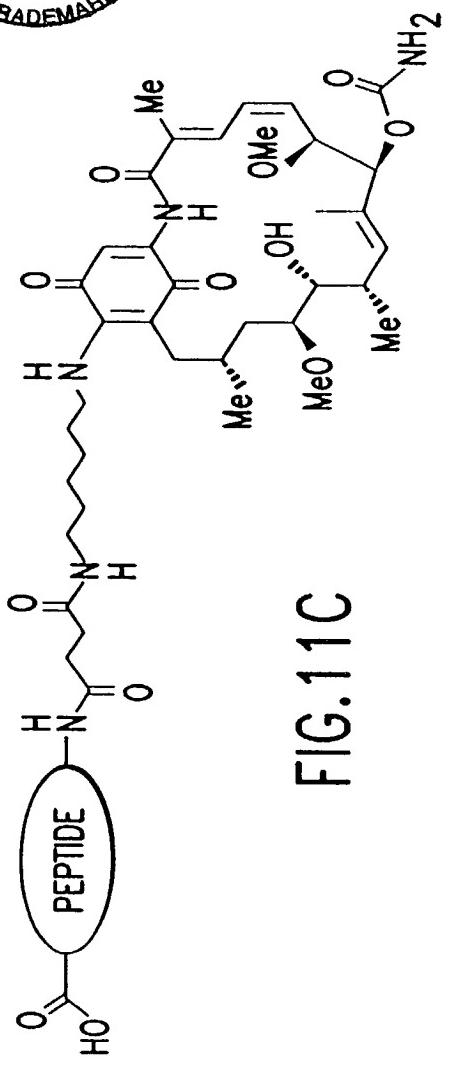


FIG. 11C

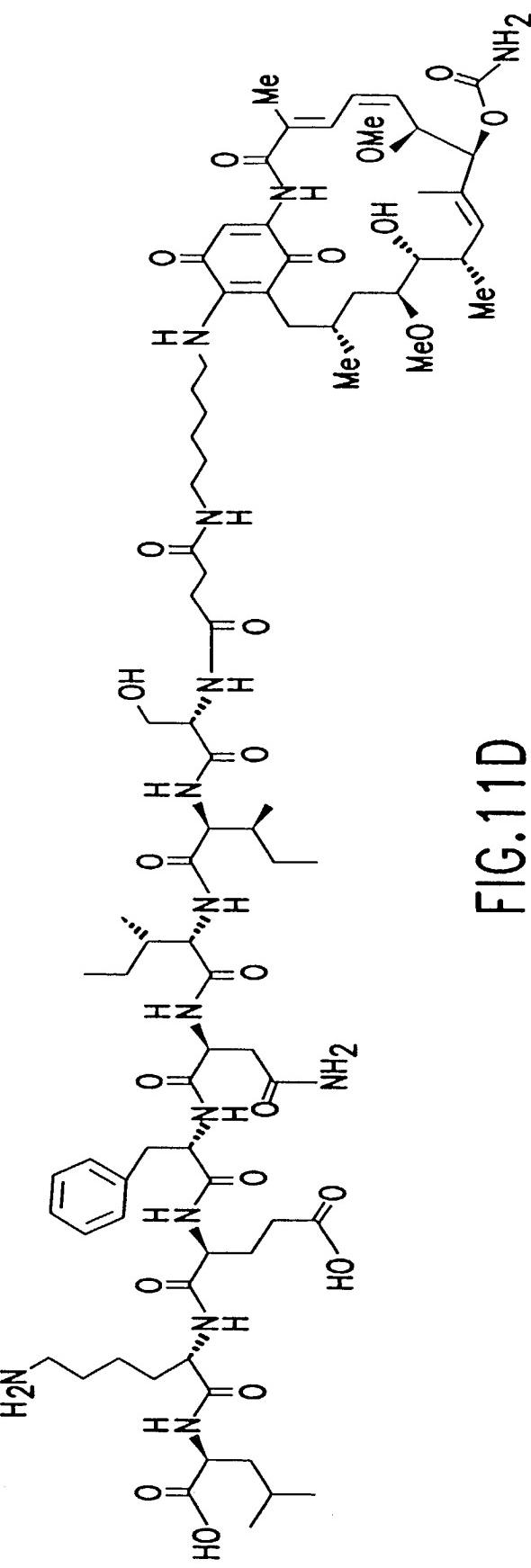


FIG. 11D

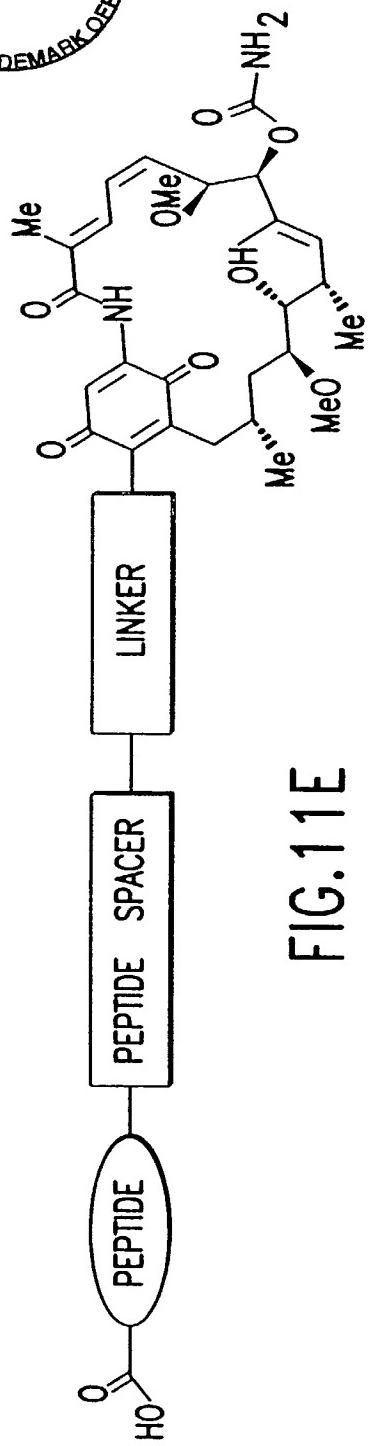


FIG. 11E

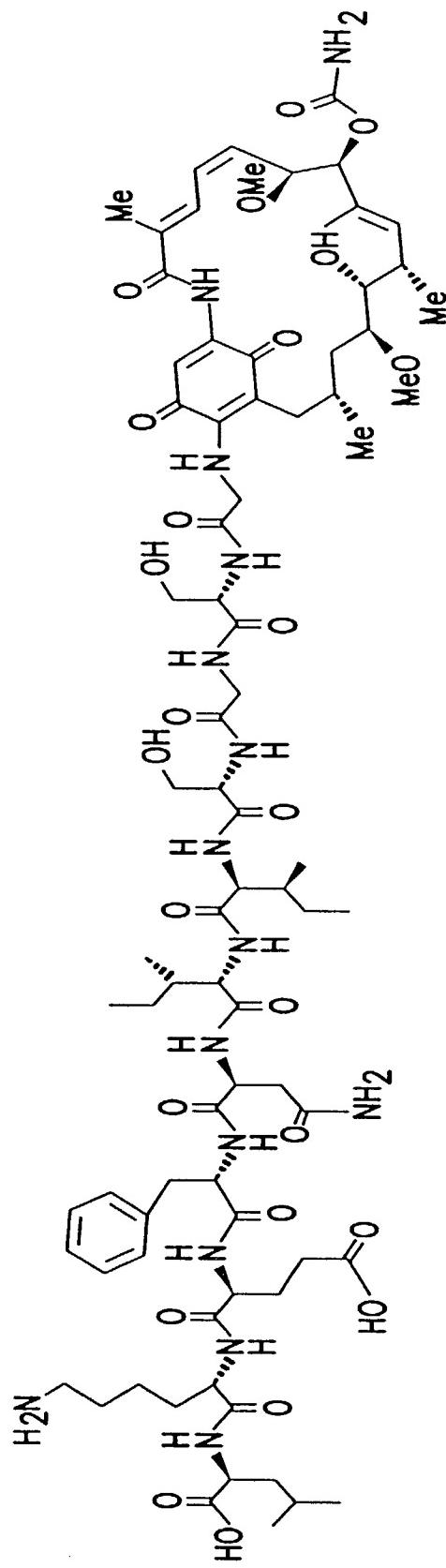


FIG. 11F



J C O E 2 3 2 2 3 2 7 2 E 3 = J C E 2 3 2 3 2 2

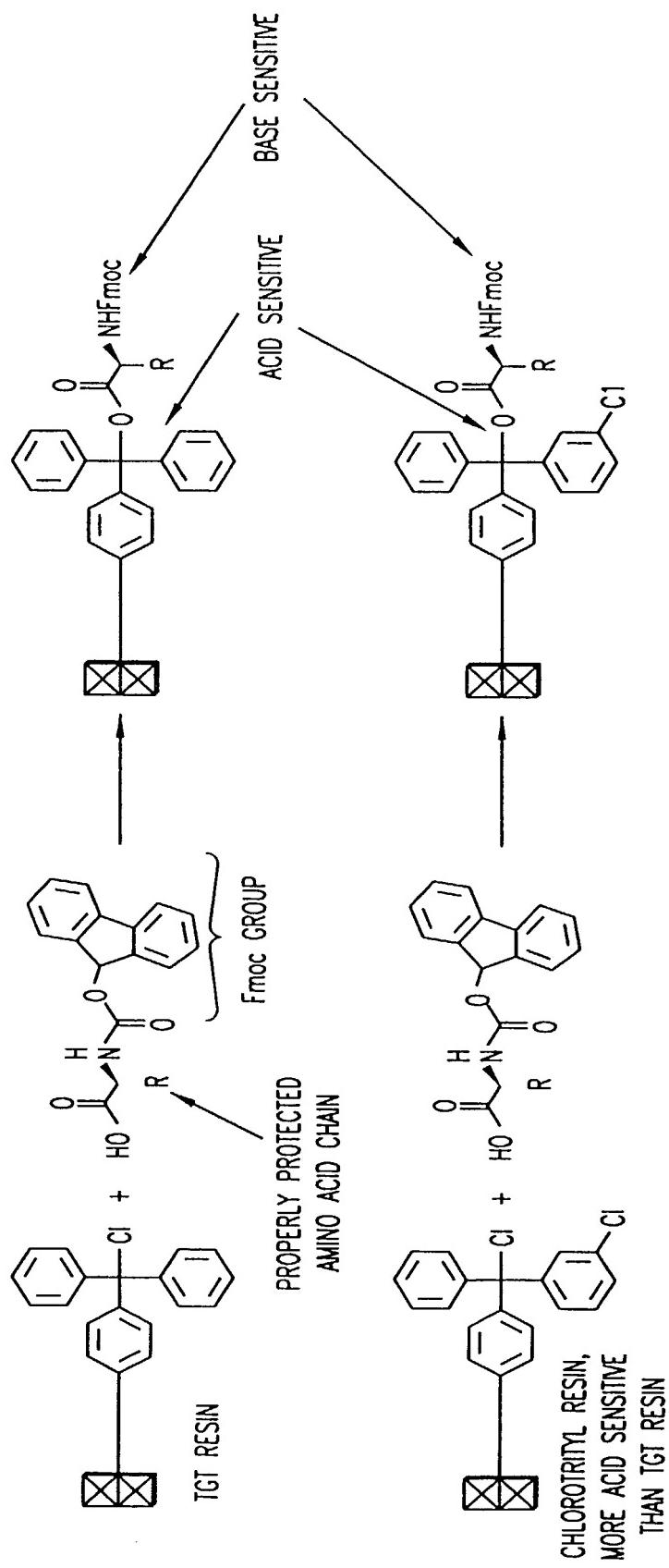


FIG. 12

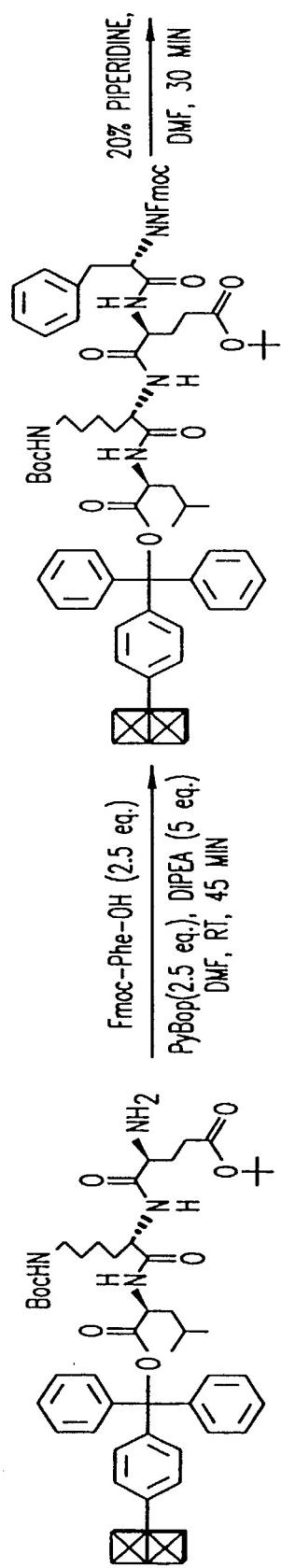
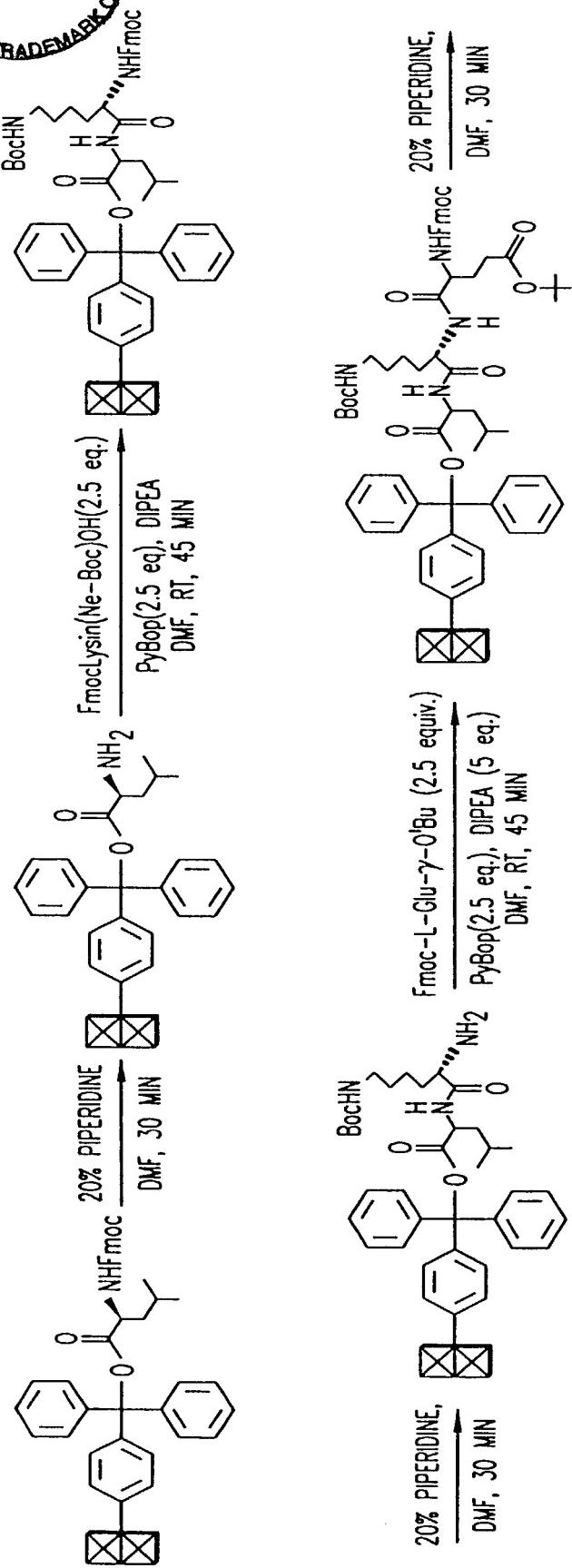
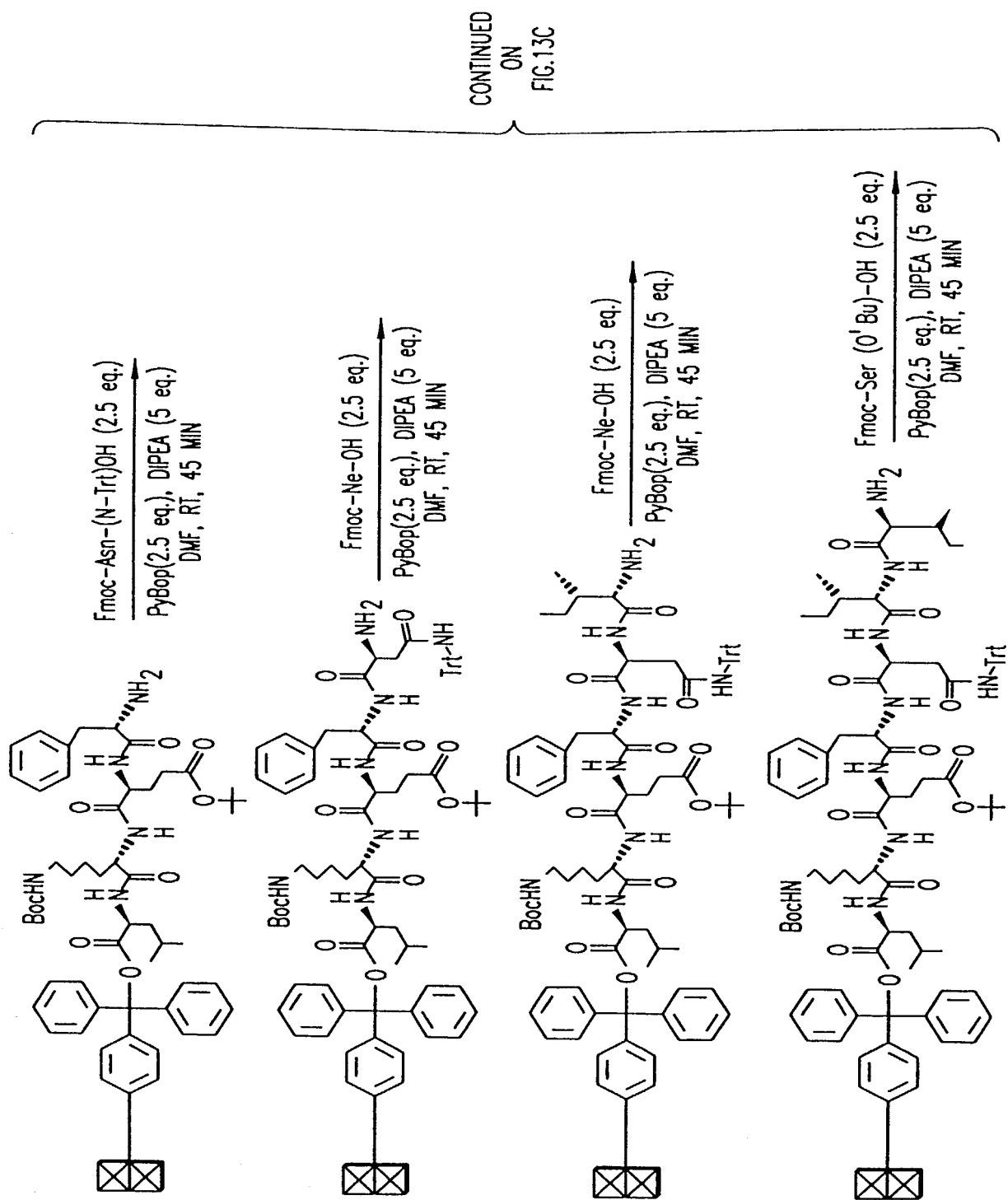


FIG. 13A



1 13 D 3 2 3 7 13 = 1 13 E 2 3 6 2

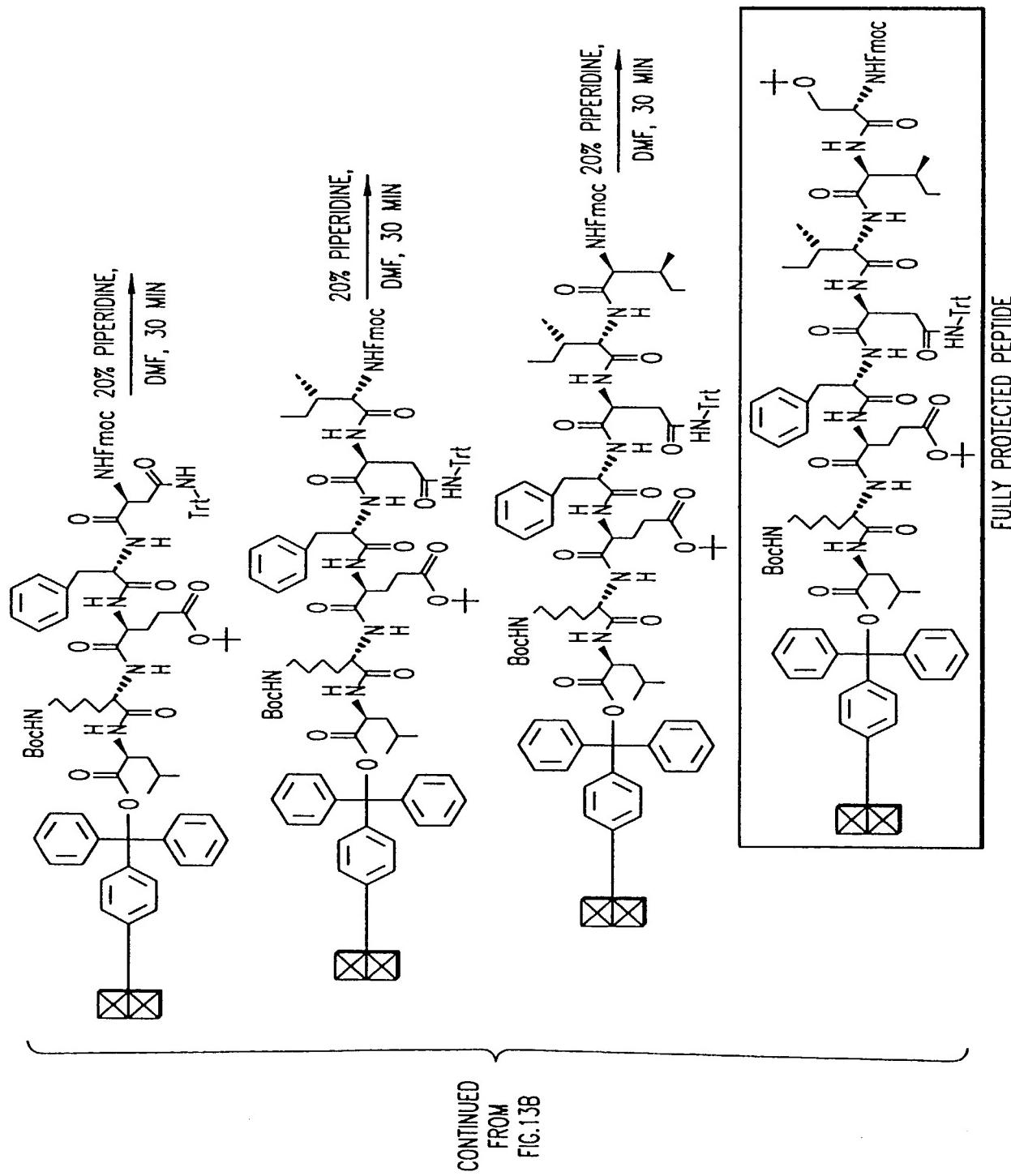
FIG. 13B



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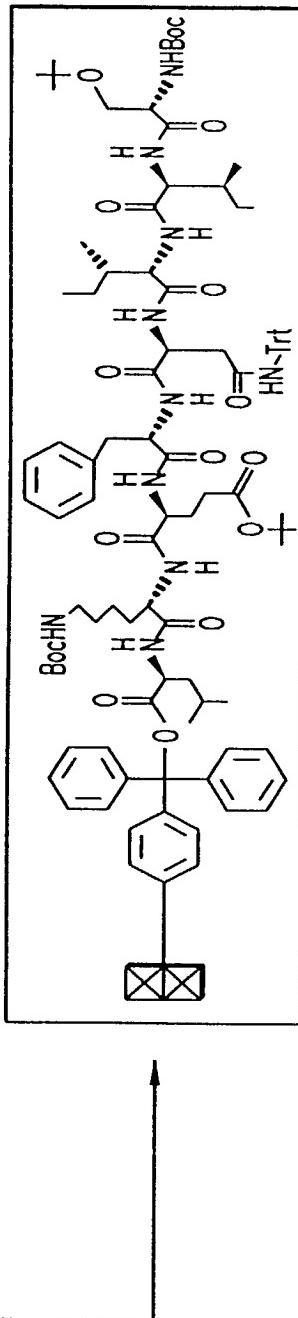
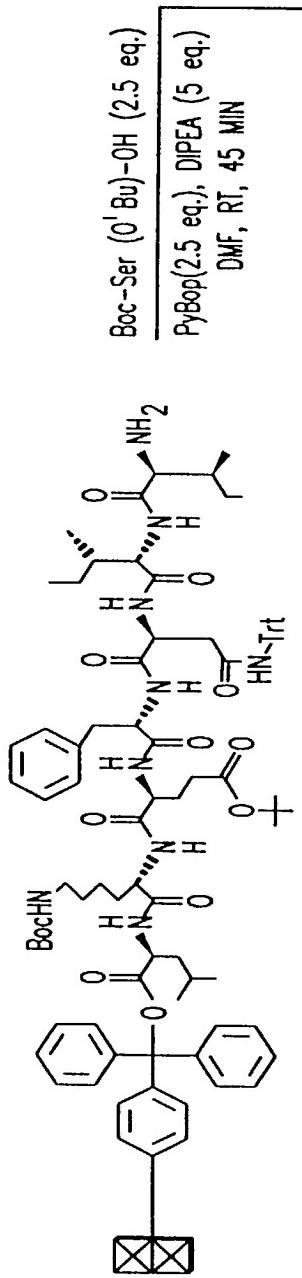


FIG. 13C





1005220202



FULLY PROTECTED PEPTIDE

FIG. 14A

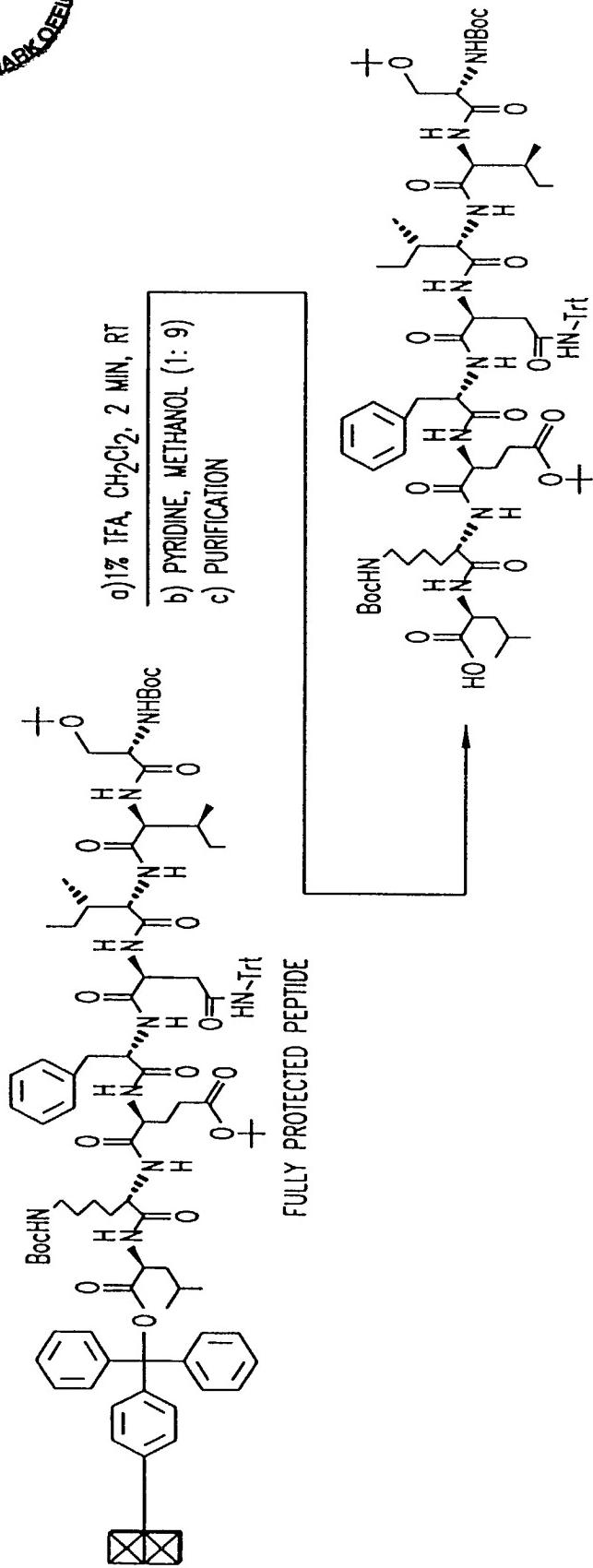
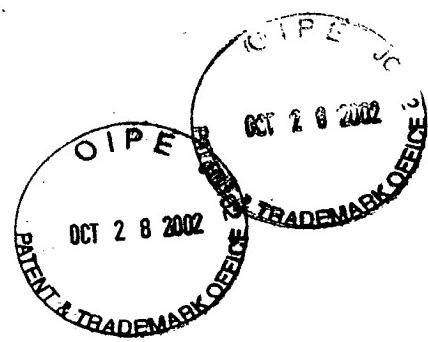
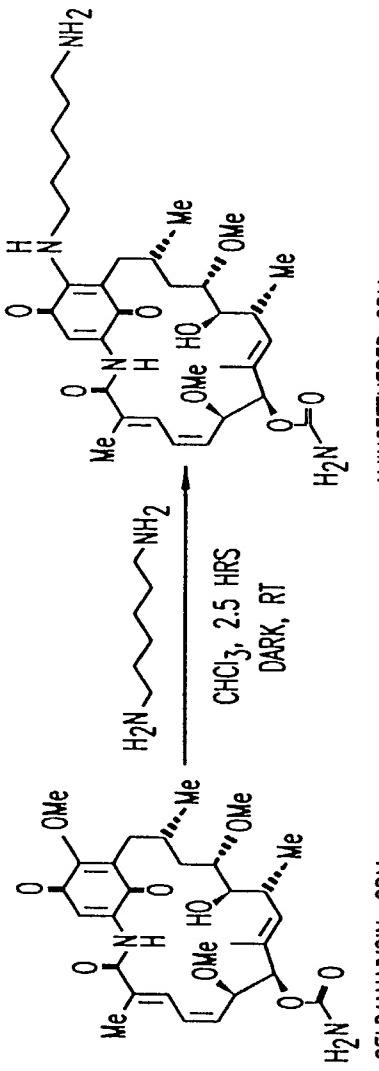


FIG. 14B

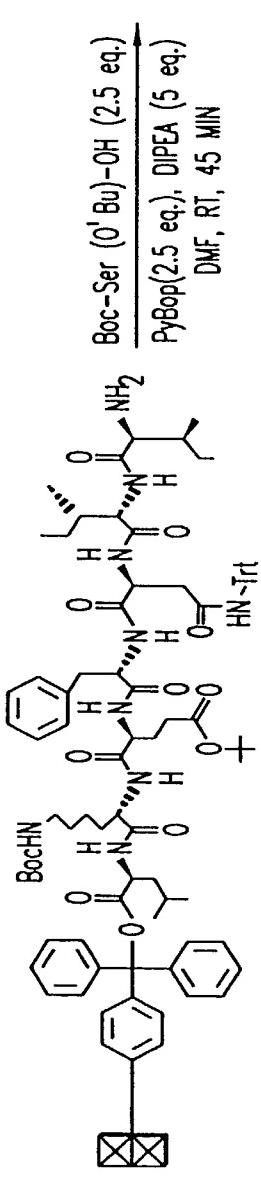


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GELDANAMYCIN, GDM AMINOTETHERED GDM

FIG. 158
CONTINUED
ON



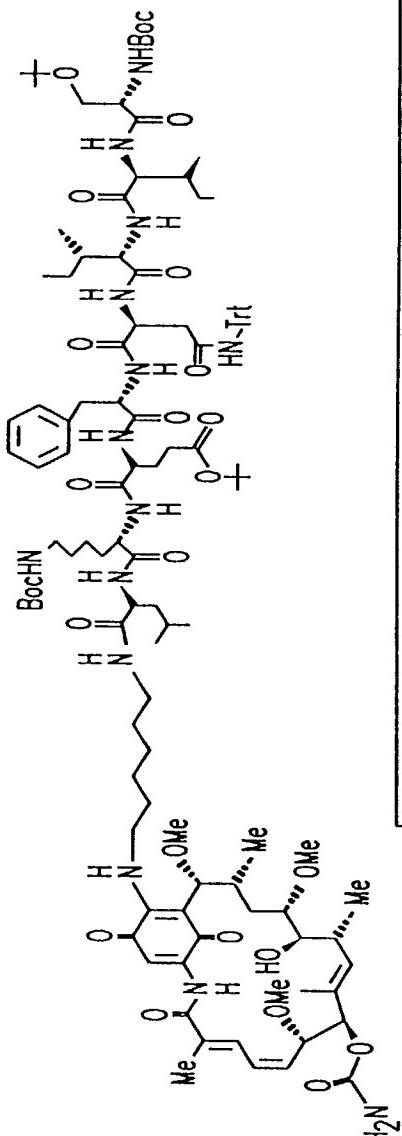
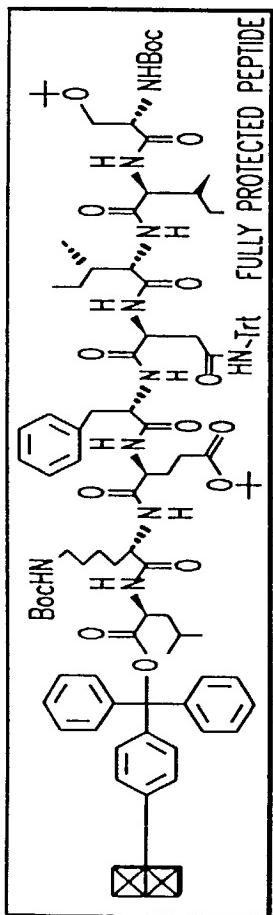
1) 1% TFA, CH_2Cl_2 , 2 MIN
 2) PYRIDINE, MeOH (1: 9)
3) FLASH CHROMATOGRAPHY
ON SILICA GEL

 a) PyBop, DIPEA, DMF
 b) AMINOTETHERED GDM

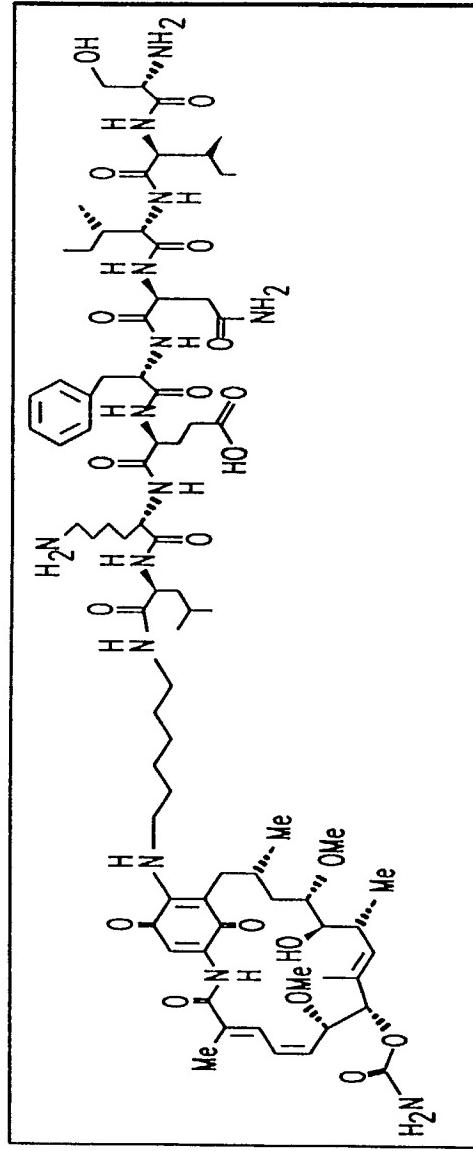
FIG. 15A



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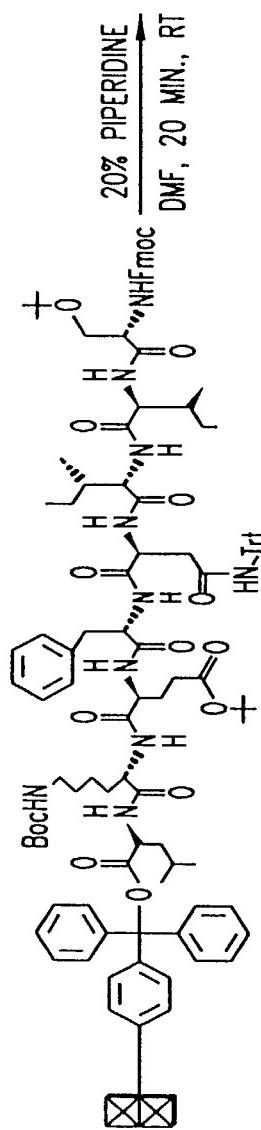


CONTINUED
FROM
FIG. 15A



- 1) DEPROTECTION:
95% TFA, 2.5% CH₂Cl₂, 2.5% TIPS
2) PURIFICATION

FIG. 15B



CONTINUED

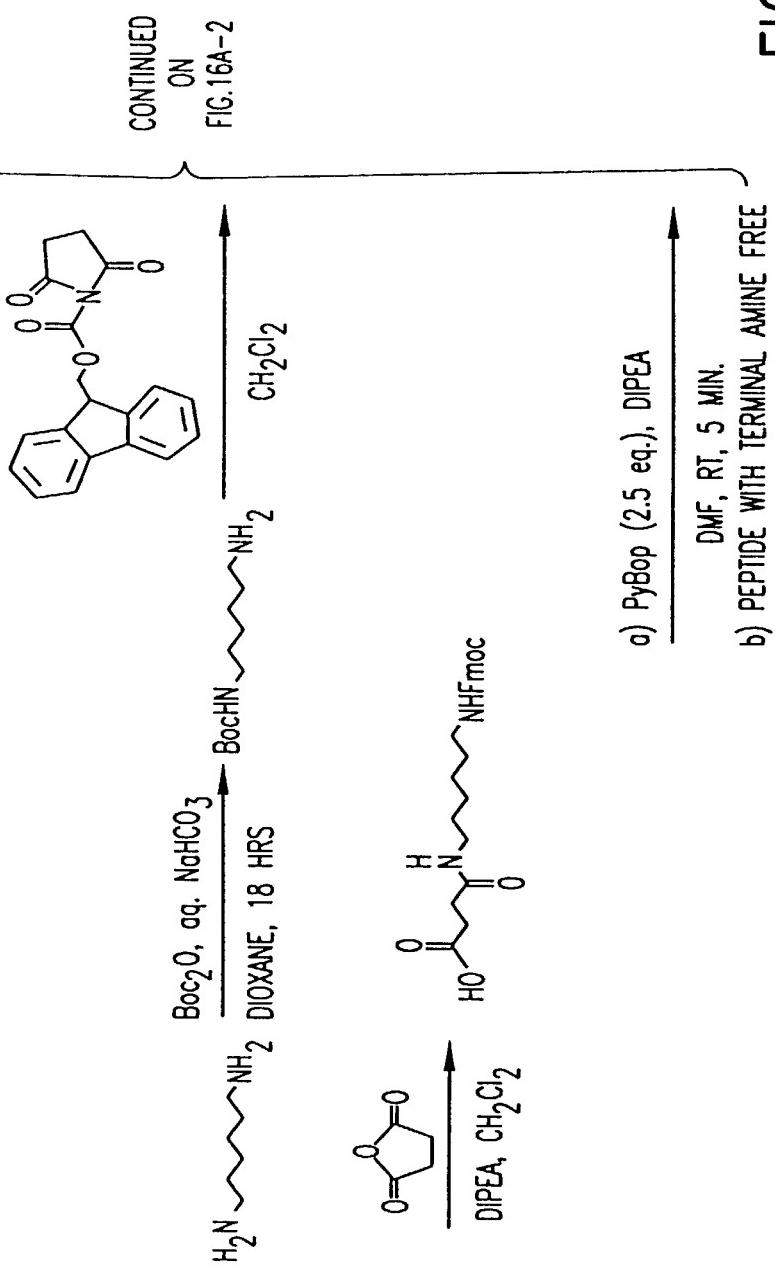
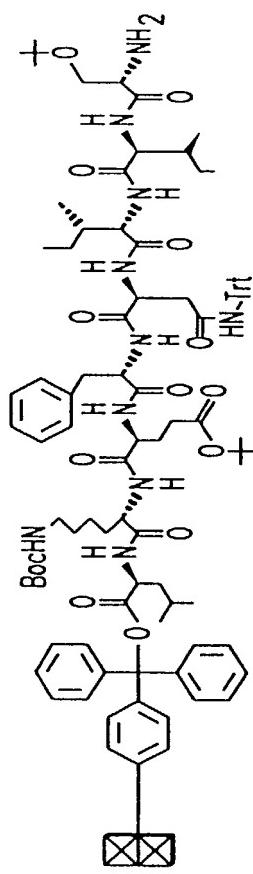


FIG. 16A-1



CONTINUED
FROM
FIG.16A-1

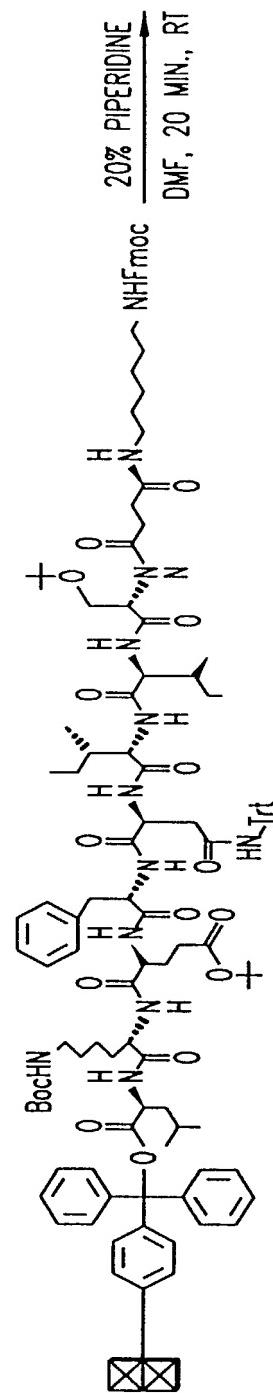
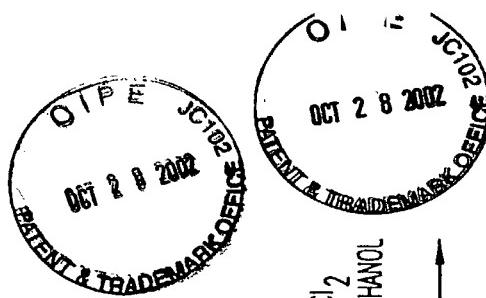


FIG.16A-2



1 0 0 0 5 2 3 7 0 3 = 1 0 0 0 6 0 0 0

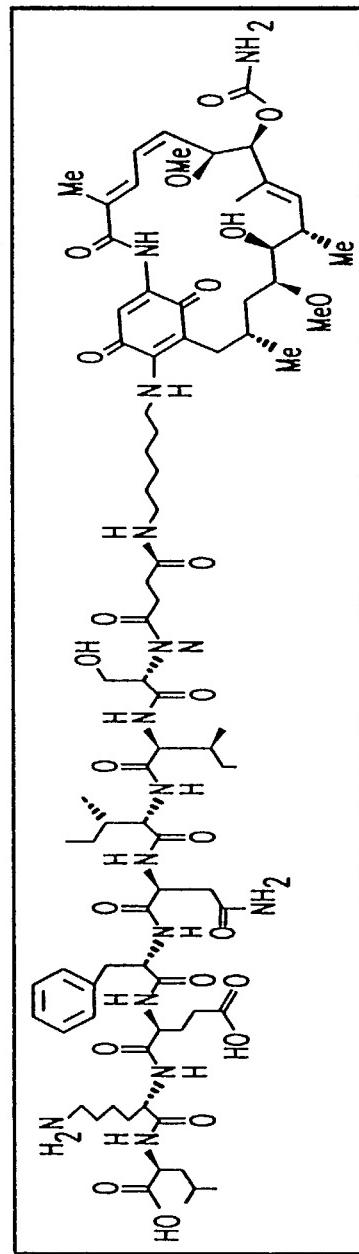
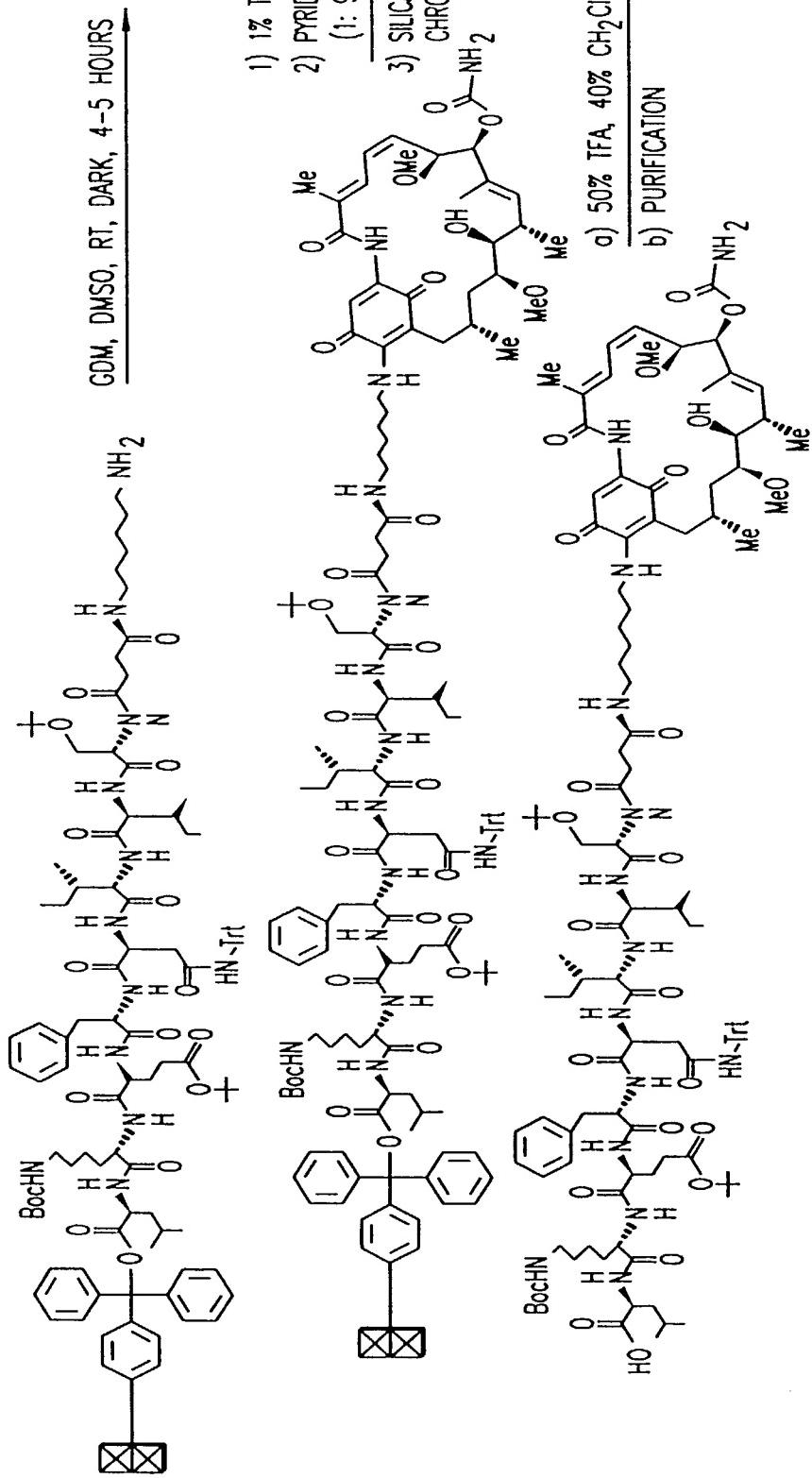


FIG. 16B

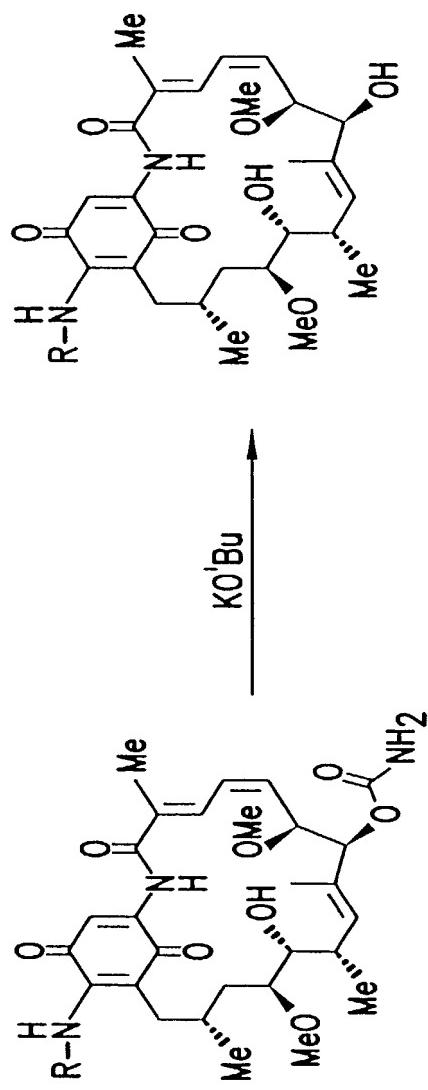


FIG. 17A

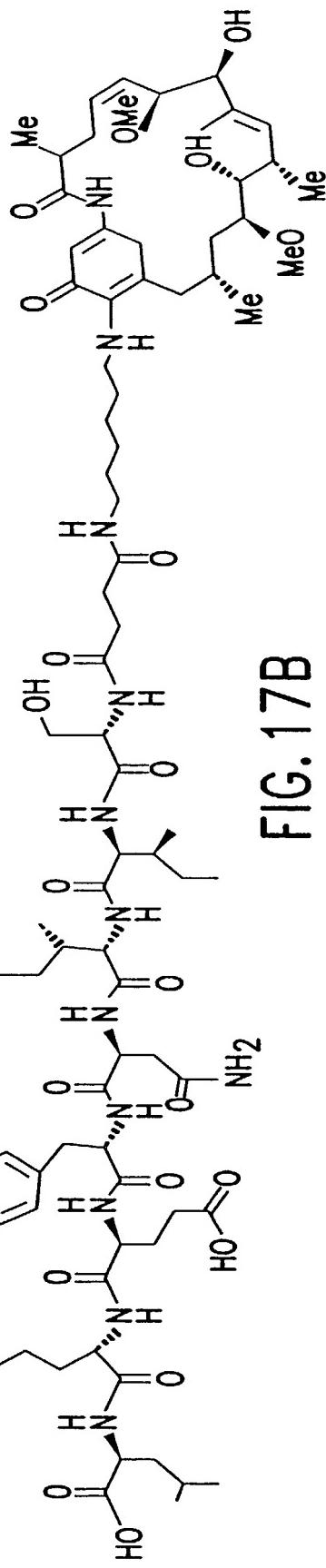


FIG. 17B

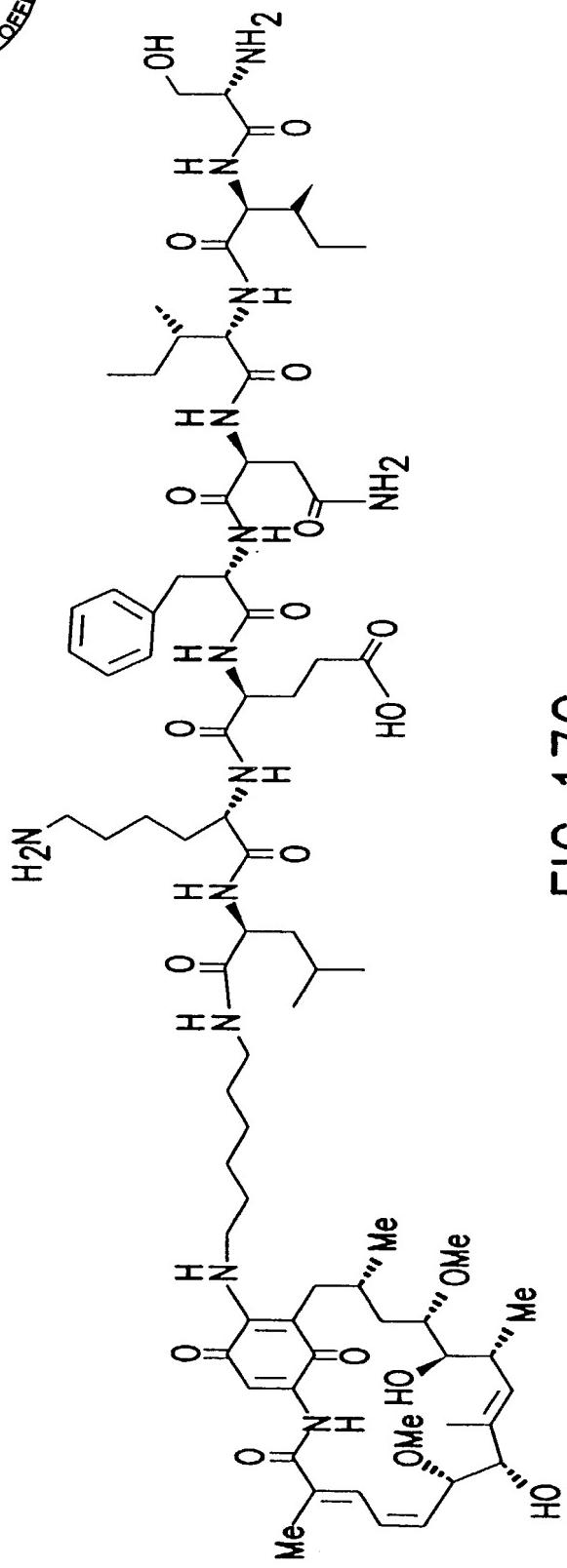


FIG. 17C

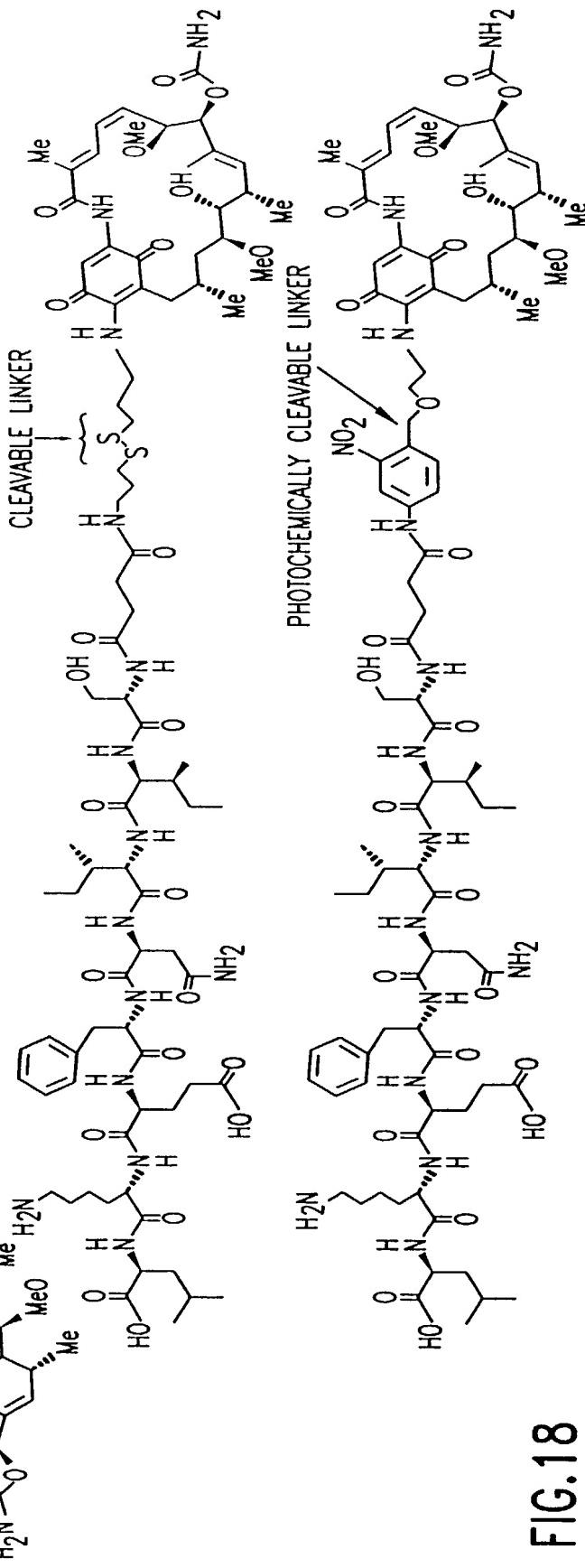
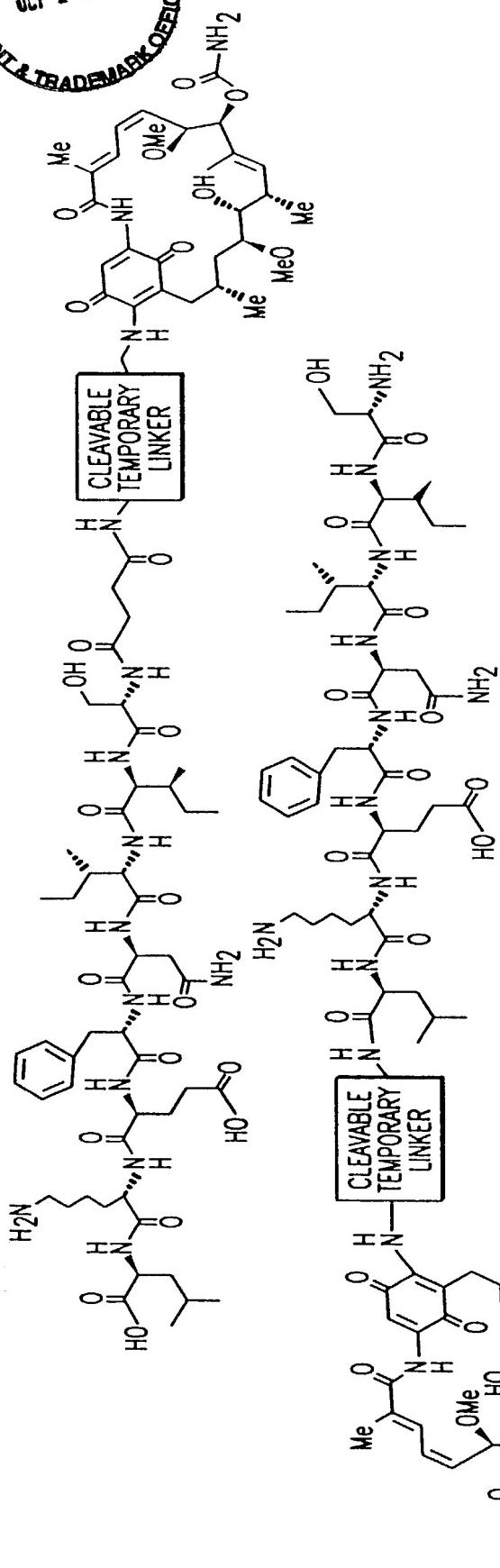
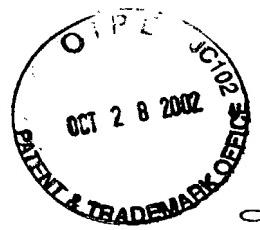


FIG. 18

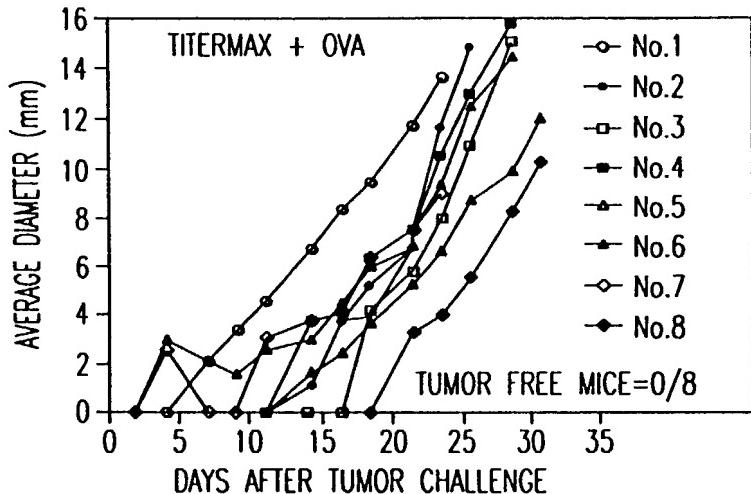


FIG.19A

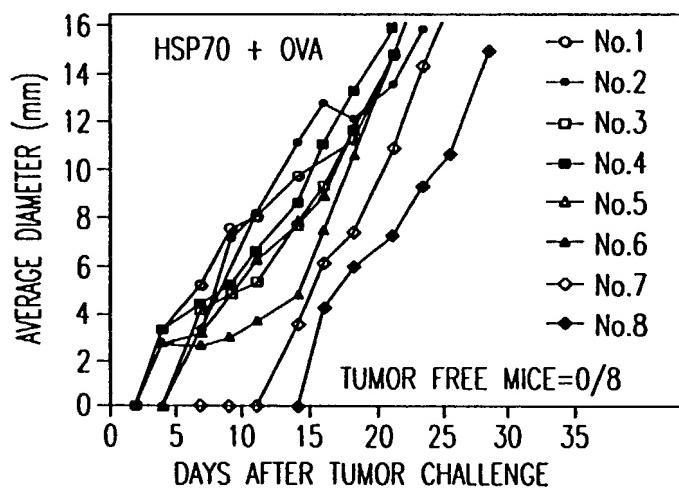


FIG.19B

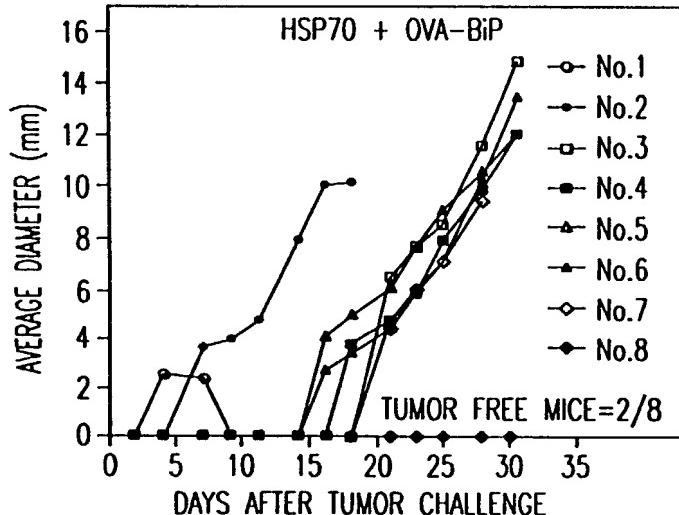


FIG.19C



J 10 C 15 E 2 15 T 23 = J 10 E 2 3 0 2

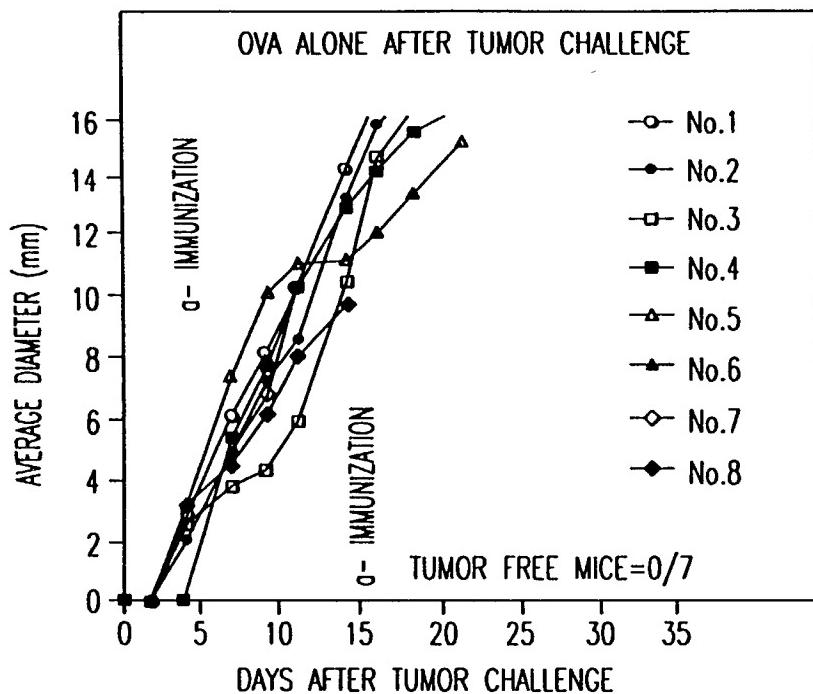


FIG.19D

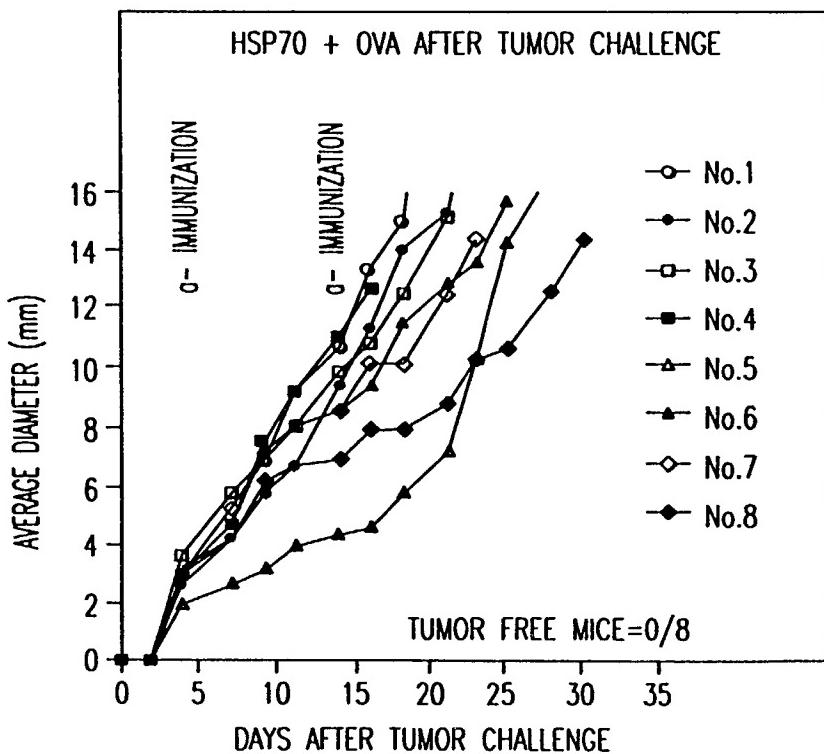


FIG.19E



1 2 3 4 5 6 7 8 9 10 11 12

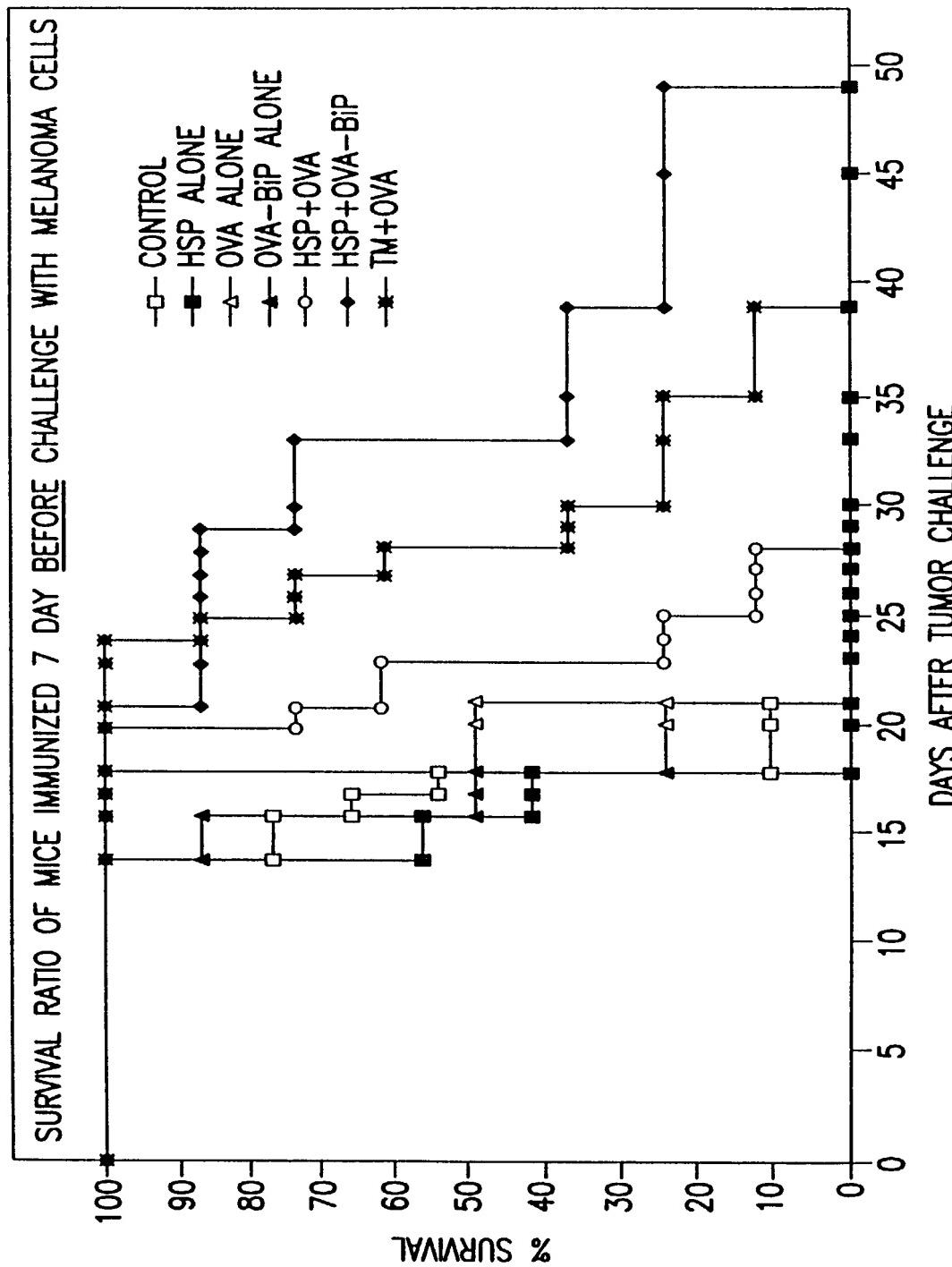


FIG. 19F



4 43 05 32 53 77 63 .. 1 43 23 34 02

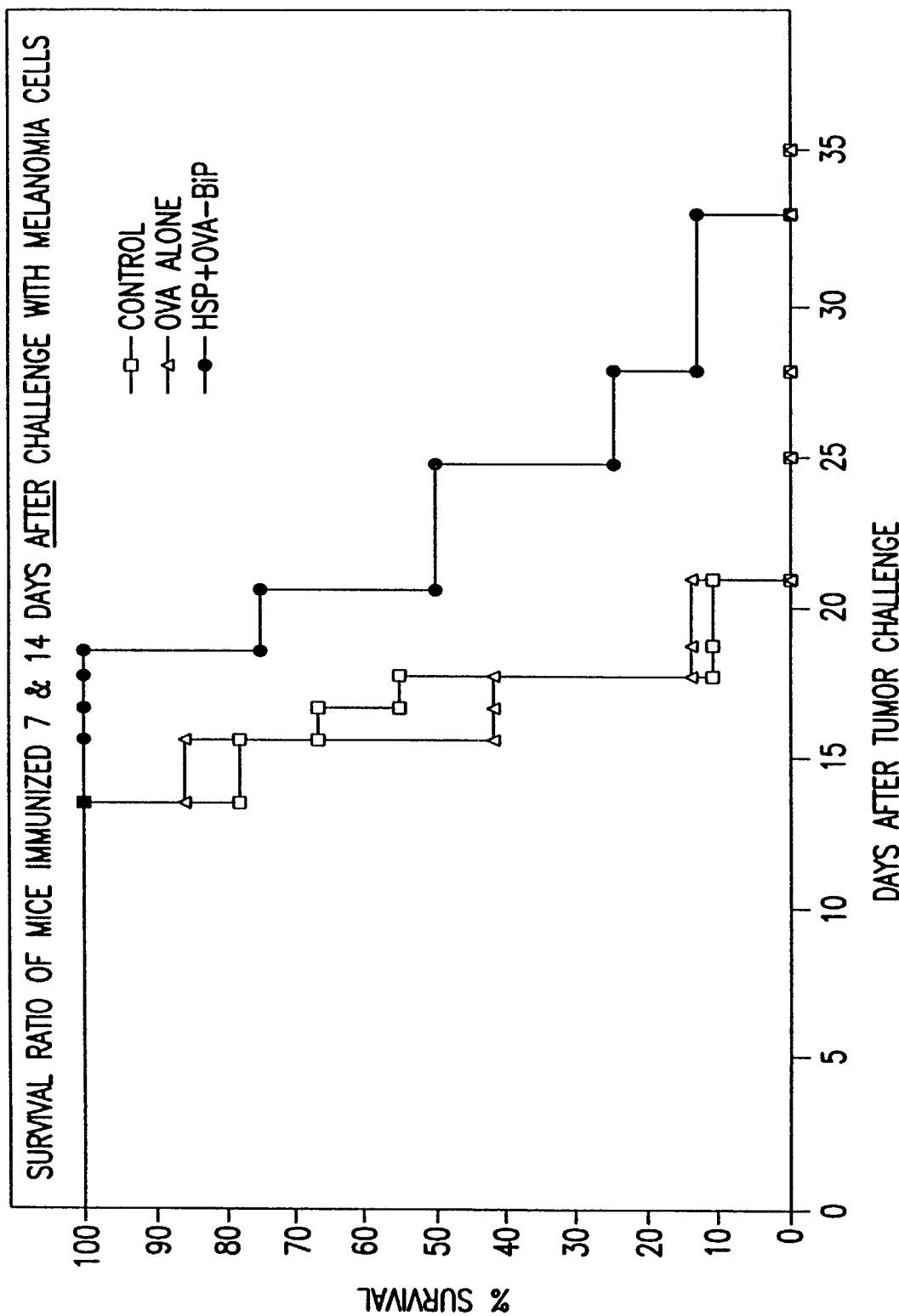


FIG. 19G